THE JOURNAL
of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 164, NO. 8 — CHICAGO, ILLINOIS — JUNE 22, 1957
COPYRIGHT, 1957, BY AMERICAN MEDICAL ASSOCIATION

CARDIAC ASYSTOLE

Henry S. Ruth, M.D.,† Mary L. Buckley, M.D.
and
Kenneth K. Keown, M.D., Philadelphia

• *Experience with anesthesia in all types of surgery has led to the conclusion that the cause of fatalities is to be sought not so much in the chemical identity of any given anesthetic as in errors incidental to its administration. Statistics indicate that cardiac arrest is sufficiently frequent to call for a study of the factors likely to precipitate it. A list of 10 such factors is given, including especially hypoxia, hypercapnia, excessive anxiety in the patient, and errors in dosage. Most of these are preventable by carrying out the protective measures here described. If cardiac arrest occurs it must be treated at once. Thoratocomy by a long intercostal incision in the fourth, fifth, or sixth left interspace should be done quickly to permit maintenance of circulation by direct manual rhythmic compression of the heart through the intact pericardium. Promptness is more important than asepsis, and no intrathoracic infections have been reported in patients who survived such emergency thoracotomies. Artificial respiration by positive pressure must be maintained while the thorax is open. If the heart is found not in a state of asystole but in ventricular fibrillation, rhythmic manual compression must be continued to prevent acute dilatation, but in addition the heart must be brought to a standstill electrically by applying a defibrillating current before there is any possibility of restoring the normal sinus rhythm. The procedures here presented have saved 60% of patients who developed cardiac asystole during anesthesia.*

The literature on cardiac asystole appears contradictory and controversial to the interested reader. We shall attempt to clarify the problem by outlining the salient practical aspects. Both the literature and our own experiences, which are based on an anesthesiological practice for all types of surgery, provide the background.

Cardiac asystole, cardiac arrest, and cardiac standstill are terms that have been used, interchangeably, to designate a cessation of heart action, implying its occurrence during the course of anesthesia and surgery. This situation can occur without warning, or when a heart lesion or multiple heart lesions have been recognized prior to the induction of anesthesia. Untreated, cardiac asystole terminates promptly in death.

According to our survey, the first reference in the literature to lifesaving procedures applicable in this acute situation was recorded by Tuffier in 1898.[1] Few additional contributions appeared until recently. Perhaps the earlier fear of opening the thoracic cavity and, later, a lack of knowledge of the basic concepts of the procedure and its possibilities were the accountable factors.

Statistics compiled by various authors show that the incidence of deaths in the operating room varies from 1 in 804 [2] to 1 in 1,858 [3] anesthetics administered. Literature has been prone to cite the anesthetic agent and method employed when these fatalities occur. It is now the belief that anesthetic agents per se are not usually the responsible etiological factors, but that errors incidental to their administration, as well as other factors, are more frequently the cause for these fatalities.[4] Nevertheless, these statistics provide some conception of the number of instances in which treatment of cardiac arrest may be indicated, and in some of them treatment will be successful.

Causes of Cardiac Asystole

We believe that 2 or more of the following 10 conditions are present prior to or when cardiac asystole occurs.

From the Department of Anesthesiology, Hahnemann Medical College and Hospital.
†Dr. Ruth died June 7, 1956.

1. Anemia and decreased circulating fluid volume. Inadequate oxygen-carrying capacity of the blood is well known as a cause of major dysfunctions of both heart and brain.

2. Overdose of anesthetic agent. Effects of this on the respiratory centers or the vasomotor center, or both, can result in secondary heart failure.

3. Anxiety of the patient. Increased epinephrine outflow sensitizes the myocardium to cardiac arrhythmias.

4. Increased carbon dioxide level in the blood. The ensuing chemical imbalance may cause respiratory depression and cardiac dilatation.

5. Cardiac and cardiovascular valvular diseases, acquired or congenital. Both the type and the degree of involvement determine their potentialities.

6. Hypoxia, either acute and pronounced or chronic in form, as found in long-standing pulmonary diseases. Efficient oxygenation at all times is a basic concept of acceptable anesthetic practice.

7. Inadvertent administration of an undesirable drug or inaccurate dosage of the correct drug. A careful check of the label of the container before administration of a drug is fundamental and its importance is generally known, but rechecking may be neglected in the face of an emergency.

8. Unrecognized administration of an unindicated and harmful compressed gas. Labels on gas cylinders, as well as on containers for drugs, require identification before administration.

9. Cardiovascular effects of anesthesia or surgery. Reflexes (possibly vagal in origin), postural changes producing torsion of the heart and great vessels, and mechanical pressure on the coronary vessels by surgical manipulations are all prominent in producing undesirable effects.[5]

10. Certain endocrine and metabolic disturbances. These may be present but unrecognized when emergency surgery does not allow time for the usual thorough preoperative physical examination.

Cardiac arrests that occur early in anesthesia are usually due to errors in the anesthetic technique, anxiety complex of the patient, valvular heart disease (particularly aortic stenosis and mitral regurgitation), hypoxia, or cardiac reflexes, such as vagal response elicited by the insertion of an airway. For example, May and others [6] performed cardiac catheterizations on patients under basal conditions and repeated them under conditions of excitement. They found, by comparison, that an apprehensive individual exhibits a materially increased cardiac output, with coincidental increased cardiac effort.

We believe that, when a patient with an impaired myocardium or marked valvular defect arrives for surgery in a state of excessive apprehension, it is advisable to postpone the surgery. The importance of anxiety and its detrimental effect on the patient can be demonstrated by our experiences.[7] Five patients with severe mitral stenosis who had shown no pulmonary edema immediately preoperatively arrived in surgery; however, induction of anesthesia unavoidably was somewhat delayed by factors beyond our control. In this short interval of delay, acute pulmonary edema developed, which we interpreted to be precipitated by fear. Surgery was canceled, and the patients returned to their rooms, receiving oxygen by means of a positive-pressure mask. Later, when anesthesia was induced by intravenous injection of thiopental sodium given in the patient's room without informing him that he was rescheduled for surgery, each patient survived both anesthesia and surgery uneventfully. To the best of our knowledge, protection from fright was the only variable between the original and second attempts at surgery.

Cardiac standstill may occur at any time during the course of anesthesia. The most frequent periods for its occurrence are those of induction and emergence, unless shock or surgical complications are present during the maintenance period.

Asystole occurring late in the anesthetic period or during emergence from anesthesia may be due to anemia or decreased volume of circulating blood from unrecognized surgical blood loss; late effects of overdosage of anesthetic agents; carbon dioxide excess; hypoxia; reflexes initiated by extubation, aspiration of the tracheobronchial tree, or stimulation by a mechanical airway; or a sudden postural change of the anesthetized patient.[8]

Additional causes for asystole may be considered applicable by others. We have attempted to call attention definitely to those we are certain have been predisposing factors in our analysis of our own experiences as well as the reports of others.

Protective Measures

There are certain requirements of major importance that should be provided to protect against the occurrence of asystole. Some may appear to be trite, but because of this very fact they may be neglected. They are as follows:

1. A well-trained anesthesiologist is essential to the best interests of the patient whenever possible, but especially for the types of surgery where cardiac arrest occurs more frequently, as in intracardiac surgery. He should be one in whom both the surgeon and the patient have confidence and who is well informed of the pertinent normal and abnormal physiology coincidental with the course of surgery and anesthesia.

2. The indication for a thorough preanesthetic physical examination and evaluation of handicapped patients, especially, requires no emphasis here. Preoperative correction of any associated condition for which surgery will not be curative should be attempted in all elective procedures.

3. Adequate preliminary medication is essential to allay fear, but oversedation, which depresses the vital centers of respiration and circulation, is to be avoided.

4. Last-minute cancellation of surgery should be considered always if evidence is observed that the medical preparation of the patient is not as adequate as anticipated. Such cancellation should be decided by mutual agreement between the surgeon and the anesthesiologist. The cancellation may tax the relationship of surgeon and anesthesiologist unless there exists a mutual respect between them. It is unfortunate, but not too uncommon, that a patient's life is lost if good advice is not heeded or if the anesthesi-

ologist is not willing to assert his knowledge in the patient's best interest. Contrariwise, an overbold anesthetist may encourage a reasonable surgeon to take needless risks.

5. Constant accurate evaluation of the status of anesthetized patients is important at all times. This is emphasized by a realization that asystole can occur suddenly in patients under the direction of any anesthesiologist.

6. Even though only a suspicion of cardiac arrest exists, no time should be lost. Nothing will be accomplished by rechecking blood pressures that have been nonexistent for two or three minutes, at least until corrective treatment has been started. When there is no palpable pulsation of the carotid artery, cardiac action is immediately assumed to have ceased.[9]

7. A well-organized plan of action must be developed for the management of cardiac asystole if results are to be satisfactory. No time should be consumed by discussions of the situation by members of the operating team.[9] First, the surgeon is informed that the patient's condition is precarious. When the carotid pulse becomes imperceptible, the anesthetist should firmly announce that evidence of heart action is not demonstrable. If hesitation ensues, the anesthesiologist should provoke definitive action by the question, "Will you open the chest or shall I?" Even a timid individual will then act, or request action by the anesthesiologist.

8. The presence of proper equipment should be ascertained prior to the induction of anesthesia. The essential items to be checked are a laryngoscope that will function; endotracheal catheters; solutions of atropine sulfate, epinephrine, and procaine hydrochloride; and appropriate syringes and needles.

9. The training of all, or as many as possible, of the personnel in the departments of surgery and anesthesiology in the proper method of cardiac resuscitation is important. Thereby, many physicians will be able, quickly and efficiently, to open the chest and attempt restoration of cardiac action, without trauma to the heart itself, and with a possibility of success.

In certain cases there are premonitory evidences of impending cardiac failure and subsequent standstill. These include slowing, with a weakening of the pulse, as well as hypotension and cyanosis. When these signs appear, every attempt to oxygenate the patient adequately should be instituted. If the volume or concentration of oxygen delivered to the alveoli is inadequate, higher concentrations will be beneficial. If the increased oxygen tension of the inspired gases and inflation of the lungs do not correct the condition, and also fail to produce a prompt increase of rate and force of cardiac action in the absence of respiratory obstruction, atropine sulfate, 1/100 grain (0.6 mg.), should be administered promptly and intravenously. This drug should bring about the desired responses, in instances associated with reflex cardiac inhibition, by decreasing vagal outflow. Failure to obtain a full, strong pulse, with continuation of the hypotensive state, after the administration of oxygen and atropine sulfate would indicate the immediate use of methoxamine (Vasoxyl) hydrochloride, 20-40 mg., in a solution of 500 cc. of 5% dextrose and water, administered at the rate of 60 to 90 drops per minute. If all three measures fail, the drug of choice is epinephrine 1:1,000, 0.25 cc. of the 1:1,000 concentration as the original dose, administered intravenously. It should be realized that, most commonly, asystole occurs after a period, no matter how brief, of slowing and weakening of rhythmic cardiac contractions.

On the other hand, a more rare but more serious condition of ventricular fibrillation may develop. Ventricular fibrillation commonly follows episodes of ventricular tachycardia and hypotension. When the existence of a very rapid heart rate plus falling blood pressure is recognized, the anesthesiologist should find procaine hydrochloride or, at times, procainamide (Pronestyl) hydrochloride effective in slowing the ventricular rate and decreasing the irritability of the ventricle. Methoxamine, because of its ability to slow the heart rate while elevating the systemic blood pressure, has also proved invaluable in this condition.

Cardiac Compression

Various methods of cardiac compression are advocated by writers on the subject. Hamilton Bailey,[9] Hyde and Moore,[10] and Wolff [11] have reported on patients who have survived asystole after manual compression of the heart via the abdominodiaphragmatic approach. We believe, with the majority (including Beck,[5c] Dripps, Kirby, and Johnson,[12] Rizucka,[31] and C. P. Bailey,[14]) that the efficient anatomic approach to compression of the heart is obtained by left thoracotomy.

In reviewing the literature on cardiac asystole, we were unable to find a report of a surviving patient who subsequently developed an infection of the chest wall, pleura, or pericardium. The reason for this is obscure, but such information emphasizes the fact that valuable time should not be consumed by scrubbing, gowning, or preparing the chest wall with an antiseptic solution. The most important factor for survival is the speed with which the chest is opened and effective compression of the heart begun. We advise and employ a long intercostal incision in the fourth, fifth, or sixth interspace on the left, which is accomplished easily by making the incision directly beneath the mammary gland.

When the chest is opened, inspection will reveal whether the heart is at a complete standstill, is still contracting weakly, or is in a state of ventricular fibrillation. Under any of these conditions the lung is compressed posteriorly, the fingers of the right hand are placed under (posterior to) the heart, with the pericardium intact, and the thumb is placed over the most prominent portion of the anterior aspect of the ventricle. The heart is compressed between the thumb and the fingers, expelling a quantity of blood into the great vessel with each compression. In instances where the heart has ceased to contract immediately before thoracotomy, or is about to cease, rhythmic compression through the intact pericardium may be sufficient to restore independent and effective cardiac action within a few seconds. If so, opening of the pericardium is not indicated, and there is no need, usually, for stimulation by drugs.

Frequently, no immediate and rapid response is obtained. If the heart reacts by contracting weakly with each compression, but does not show a tendency to develop independent contractions, it is necessary to incise the pericardium widely, usually just anterior to, and parallel with, the left phrenic nerve. The fingers of the right hand then can be inserted within the pericardium, well back of (posterior to) the ventricles. While the thumb of the same hand can be used for counterpressure on the anterior surface of the heart, a more efficient compression can be obtained by placing the fingers of the left hand within the open pericardium, too, anterior to the heart's surface. By approximating the two hands rhythmically, thereby "squeezing" the heart, the emptying of the ventricular chambers can be made nearly complete. Any synchronous myocardial contraction is a mechanical aid, as well as an indication of a favorable prognosis.

The more extensive opening of a tight pericardium, where it appears to constrict a dilated heart, may relieve the constriction and result in a prompt return to normal effective cardiac contractions. In other instances, the dilatation of the heart may increase with the release of the constriction, and a huge atonic heart result, which probably cannot be reactivated. Ouabain administered intravenously has been recommended to reduce this dilatation and is effective in some instances.

Caution must be exercised that the finger tips, lying as they do over the thin-walled ventricle, do not penetrate or puncture the myocardium. This complication occurred on two occasions in our personal experiences.

An attempt is made to rhythmically compress the heart at the most rapid rate consistent with adequate filling of the chambers. The rate is dependent, therefore, to some extent upon the refill powers of the circulation, and also upon any mechanical interference with cardiac refilling, as, for example, the position or size of the operator's hands. It is usually impossible to rhythmically and effectively compress the heart at a rate faster than 70 beats per minute. This rate, however, is definitely more effective in the restoration of normal cardiac function than a rate of 30 to 50 beats per minute, which has been recommended. The latter rate is similar to the situation present when the heart action is about to cease, as well as in heart block, and is, therefore, unphysiological.

Tone begins to return to the relaxed myocardium in patients who may recover. Within a short time the heart should begin to contract simultaneously with the stimulation of the manual compression. These contractions may become progressively stronger. The operator should then interrupt his efforts, periodically, to observe whether the heart can continue unassisted. When it does so, and when the blood pressure becomes established at an adequate level, further resuscitative efforts are unnecessary and preparations are made for the closure of the chest. In some unusual circumstances, further definitive surgical measures may be justified, but, of course, no extensive elective surgery is justified under these circumstances.

Heart Stimulation

Whenever the responding heart fails to continue to maintain continuous efficient contractions after cessation of manual compression, cardiac compression should be resumed. In this situation, stimulation is necessary, obviously. Epinephrine is the most efficacious drug, although it manifests some danger of precipitating a ventricular tachycardia and fibrillation. This possibility may be obviated to a certain extent by prior administration of procaine or procainamide intravenously, after which the epinephrine can be administered in 0.3-to-0.50-cc. quantities of 1:1,000 concentration, preferably intravenously. However, if the first dose does not rapidly produce a response, or only unsustained results, a larger dose may be given, perhaps into a cardiac chamber. To date, we have not used over 5 cc. of 1:1,000 concentration of epinephrine in a cardiac chamber at one time.

Epinephrine will usually stimulate a rapid and vigorous cardiac action with a sizable rise in blood pressure. Such effects persist for only a few minutes, but the temporary marked improvement in physiology often will restore conditions where normal continuous cardiac activity may be expected with confidence.

If ventricular fibrillation develops (or if it has been produced by unwise administration of epinephrine), the entire ventricular myocardium is seen as a faintly or grossly twitching mass. This abnormal rhythm does not harm the myocardium directly, but it does consume available oxygen and nutriment. Until the abnormal rhythm is abolished, recovery cannot be expected. Therefore, rhythmic myocardial compression is essential again as a preliminary therapeutic measure to restore some degree of cardiac output and to improve coronary blood flow. By this means myocardial tone is improved and conditions are rendered more favorable to restoration of normal rhythm. Oxygenation of the circulating blood, coincidental with cardiac compression, is important both in ventricular fibrillation and in cardiac standstill. Occasionally, the heart will revert to normal rhythm during the course of the preliminary manual compression. This tendency may be increased by use of topically applied (5%) and systemically given (intravenously or intracardiacally) procaine [15]; 100-300 mg., or a continuous drip of a 0.2% solution, may be used for the intravenous administration.

In most instances, fibrillation persists and can be interrupted only by electric shock (countershock).[5c] By this treatment the entire myocardium is converted to a simultaneous refractory state through the effects of a powerful alternating electric current. If the myocardial condition has been improved by oxygenation and myocardial compression, the heart will tend to develop sinus rhythm when it recovers from the electrically induced refractory state. On the other hand, if the myocardium is severely anoxic through inadequate oxygenation, or exhibits an absence of tone due to serious organic disease or delayed or inadequate manual compression, a reversion to ventricular fibrillation may be anticipated. The latter development

requires resumption of the previous measures in more intensive form, as well as repetition of the electric shock.

We have used ordinary house current as it is obtained from the customary electrical outlet (110 volts, 60 cycle A.C., 6-10 amp.), applying it through two oval metallic electrodes to opposite sides of the heart, but there are some hearts that cannot be defibrillated with that type of electric current. An increase in voltage is not the only requirement, because such an increase may produce severe myocardial damage (burns). Application of the electrodes for an increased period of time (three to five seconds) may be more efficient, but can be ineffective, too, in some patients, especially those with very large hearts.

Frequently, when the heart has been shocked to a standstill by an electric current, rhythmic manual compression is again required, as well as continuation of all the measures utilized for treatment of the original asystole. In addition, use of epinephrine will be necessary to strengthen feeble contractions, although here, especially, that drug should be used with considerable caution, preferably after procaine protection.

Restoration of Blood Volume

While cardiac compression is being instituted, associated measures should be applied promptly and simultaneously. Administration of atropine sulfate in doses up to 1/100 grain intravenously or into a cardiac chamber may be considered a routine measure. Rapid restoration of circulating blood volume should not be neglected. The actual volume not only has been depleted, perhaps by preceding blood loss or shock, but is further reduced functionally immediately when the central circulatory mechanism (the heart) fails. This condition should be rectified by rapid intravenous infusion, or transfusion. Equipment for it always is available and frequently it is in use at the time the emergency occurs. Pressure methods may be utilized for more rapid administration of the desired substance, when indicated.

Prompt, sizable additions to the functionally or absolutely diminished blood volume may not proportionately raise the blood pressure, because the arterial system simultaneously or rapidly becomes depressed when cardiac action ceases. Therefore, arterial transfusions or infusions may provide immediate and prolonged benefit. If an impending or potential emergency is suspected, an arterial cannula or needle may be inserted in preparation for arterial administration of the appropriate fluid. Otherwise, an emergency set-up should be maintained at all times for arterial administration, and all members of the surgical team should be trained in its application for the time when the need arises.

Frequently, some valuable time will be lost in setting up the equipment and initiating an arterial method of administration. For this circumstance, we believe that a temporary clamping of the descending aorta is desirable. The procedure reduces the existing arterial tree, similar to an arterial transfusion, and therefore increases the peripheral resistance to cardiac outflow. By this mechanism, blood pressure may be restored or elevated, and cardiac action is stimulated by creating resistance to it, and by establishing an improved coronary blood flow. Usually the descending aorta may be mobilized readily low in the thorax, without injury to an intercostal branch. Application of the clamp is made gently (one-ratchet closure) with a long, weak-bladed clamp. Subsequently, this obstruction should be released temporarily, every 10 minutes, to permit some blood flow to the lower portion of the body and viscera. At times, digital compression of the aorta against the anterior aspect of the bodies of the vertebrae is sufficient.

As the chest wall is being opened, rhythmic manual compression of the breathing bag of the gas machine is begun, using pure oxygen. We utilize pressures of 20 to 40 mm. Hg to attempt to prevent pulmonary edema, but only for the inspiratory phase.

It is an advantage to insert an endotracheal catheter, but its use is not strictly necessary until heart action has returned. Because any anesthesiologist can compress a breathing bag of a gas machine 20 to 30 times a minute for 30 minutes, we rarely employ mechanical respirators. It is important, though, that the carbon dioxide absorber be in the circuit and functioning to control the carbon dioxide content of the respired gases.

Comment

We have been able to save 60% of patients developing cardiac asystole in our institution by following the procedures presented here. Cases of asystole may be with us always, but the associated mortality rate can be decreased by prompt institution of a definitive plan of action based on utilization of the information now known of the factors involved.

249 N. Broad St. (7) (Dr. Keown).

Charles P. Bailey, M.D., Philadelphia, collaborated in the preparation of the section on cardiac resuscitation.

References

1. Tuffier and Hallion, cited by Lockwood, A. L.: Surgery of Pericardium and Heart, Arch. Surg. **18**:417-474 (Jan., pt. 1) 1929.

2. Waters, R. M., and Gillespie, N. A.: Deaths in Operating Room, Anesthesiology **5**:113-128 (March) 1944.

3. Bishop, H. F.: Operating Room Deaths, Anesthesiology **7**:651-662 (Nov.) 1946.

4. Ruth, H. S.; Haugen, F. P.; and Grove, D. D.: Anesthesia Study Commission, Findings of 11 Years' Activity, J. A. M. A. **135**:881-884 (Dec. 6) 1947.

5. (*a*) Scherf, D.: Cardiac Reflexes Originating in Respiratory Tract, New York J. Med. **45**:1647-1650 (Aug. 1) 1945. (*b*) Reid, L. C., and Brace, D. E.: Irritation of Respiratory Tract and Its Reflex Effect upon Heart, Surg. Gynec. & Obst. **70**:157-162 (Feb.) 1940. (*c*) Beck, C. S.: Treatment of Cardiac Arrest, Veterans Admin. Tech. Bull. TB 10-65 **1**:1-7 (July 18) 1950.

6. May, L. G., and others: Effect of Apprehension Caused by Technical Procedures of Cardiac Output, Proc. Central Soc. Clin. Res. **21**:44-45 (Oct.) 1948.

7. Keown, K. K.; Grove, D. D.; and Ruth, H. S.: Anesthesia for Commissurotomy for Mitral Stenosis, Preliminary Report, J. A. M. A. **146**:446-450 (June 2) 1951.

8. Footnote 5*a* and *b*.

9. Bailey, H.: Cardiac Massage for Impending Death Under Anaesthesia, Brit. M. J. **2**:84-85 (July 19) 1941.

10. Hyde, T. L., and Moore, L. V.: Resuscitation After Apparent Death from Spinal Anesthesia: Effectiveness of Cardiac Massage and New Methods of Artificial Respiration, J. A. M. A. **143**:805-806 (July 1) 1950.

11. Wolff, W. I.: Cardiac Resuscitation: Complete Recovery After over Six Minutes of True Circulating Arrest, J. A. M. A. **144**:738-742 (Oct. 28) 1950.

12. Dripps, R. D.; Kirby, C. K.; Johnson, J.; and Erb, W. H.: Cardiac Resuscitation, Ann. Surg. **127**:592-604 (April) 1948.

13. Ruzicka, E. R., and Nicholson, M. J.: Cardiac Arrest Under Anesthesia, J. A. M. A. **135**:622-628 (Nov. 8) 1947.

14. Bailey, C. P.: Personal communication to the authors.

15. Mautz, F. R.: Reduction of Cardiac Irritability by Epicardial and Systemic Administration of Drugs as Protection in Cardiac Surgery, J. Thoracic Surg. **5**:612-628 (Aug.) 1936. Burstein, C.: Treatment of Acute Arrhythmias During Anesthesia by Intravenous Procaine, Anesthesiology **7**:113-121 (March) 1946.

POLIOMYELITIS IN HUSKERVILLE (LINCOLN) NEBRASKA

STUDIES INDICATING A RELATIONSHIP BETWEEN CLINICALLY SEVERE INFECTION AND PROXIMATE FECAL POLLUTION OF WATER

Paul M. Bancroft, M.D., Warren E. Engelhard, Ph.D.
and
Charles A. Evans, M.D., Ph.D., Lincoln, Neb.

• An abrupt, severe outbreak of poliomyelitis occurred in an unusually homogeneous community under circumstances permitting an analysis of possible etiological factors. During a five-week period, more than 10% of the 347 children in the area of high incidence developed poliomyelitis; 4.6% of the children suffered paralytic disease, with death or with disability lasting at least two years. During this time, there were no cases of paralytic or nonparalytic disease among the 256 children residing in the adjoining section of the village. A detailed study of the water supply revealed a close spatial correspondence between the distribution of cases and the location of flush-valve water closets not provided with vacuum breakers, as well as a temporal correspondence between the outbreak and the occurrence of extreme fluctuations of pressure in the water mains. The distribution of cases differed strikingly from the randomness observed when measles and chickenpox spread in the same community. Immunological studies further corroborated the belief that type 1 poliomyelitis virus had been carried by contaminated drinking water. It is pointed out that the testing of water at a power plant is unlikely to reveal contamination originating nearer the outlets in the community.

In 1952 a high incidence of poliomyelitis prevailed throughout the United States, with the greatest intensity in the Middle West. The state of Nebraska had a reported incidence of approximately 150 cases per 100,000, the highest incidence in the 48 states. Lancaster county, Nebraska, had a reported incidence of approximately 200 cases per 100,000, being second only to Woodbury county, Iowa, which had an incidence of 358 per 100,000.

Coincident with the onset of the epidemic in Lincoln, Neb., the disease appeared in Huskerville, 8 miles away. It was evident to both professional and lay observers that the outbreak in Huskerville was more abrupt and more intense and ran a shorter course.

The startling fact that stimulated this study was the observation, first made and widely recognized by the laymen living in the area, that, during a five-week period from June 20 to July 27, poliomyelitis (paralytic disease) did not occur in one row of residential buildings or in one-half of an adjoining row, whereas the disease did occur with remarkable frequency in the other two and one-half rows. Our study thoroughly confirmed this lay observation and led us to suggest a hypothesis to explain it.

During a five-week period, more than 10% of the 347 children in the area of high incidence developed poliomyelitis; 4.6% of the children suffered paralytic disease, with death or with disability lasting at least two years. During this time, there were no cases of paralytic or nonparalytic disease among the 256 children residing in the adjoining section of the village.

Physical Plan of Huskerville

The Lincoln Army Air Corps base hospital from World War II was converted in 1946 into a low-cost housing area for married veterans of World War II attending the University of Nebraska under the provisions of the G. I. bill of rights. It came to be designated as "Huskerville."

The buildings were uniform military barracks. As shown in figure 1, they were arranged in four symmetrical rows, separated by paved streets. Good, all-weather, elevated walkways ran the length of each row, and in the central area was a single north-south cross walk providing the only convenient passage between the rows. These buildings had been divided into from three to five apartments. Each had a combined living room and kitchenette and a modern toilet and bath, and there were usually two bedrooms. All were heated, and all received their hot water from a

From the Department of Pediatrics, School of Medicine, University of Nebraska, Omaha (Dr. Bancroft), the Department of Bacteriology, University of Nebraska, Lincoln (Dr. Engelhard), and the Department of Microbiology, University of Washington, Seattle (Dr. Evans).

local central heating plant. Cold water was supplied through mains from the Lincoln municipal water plant. The sewage disposal system was of modern design and was connected with the Lincoln municipal disposal plant.

The rectangular area on which the hospital was constructed is 1,000 by 1,700 ft., approximately one-sixteenth of a square mile. It had been reduced to a level plain, with a gentle slope to the east, the elevation at the eastern edge being 25 ft. below that on the west edge.

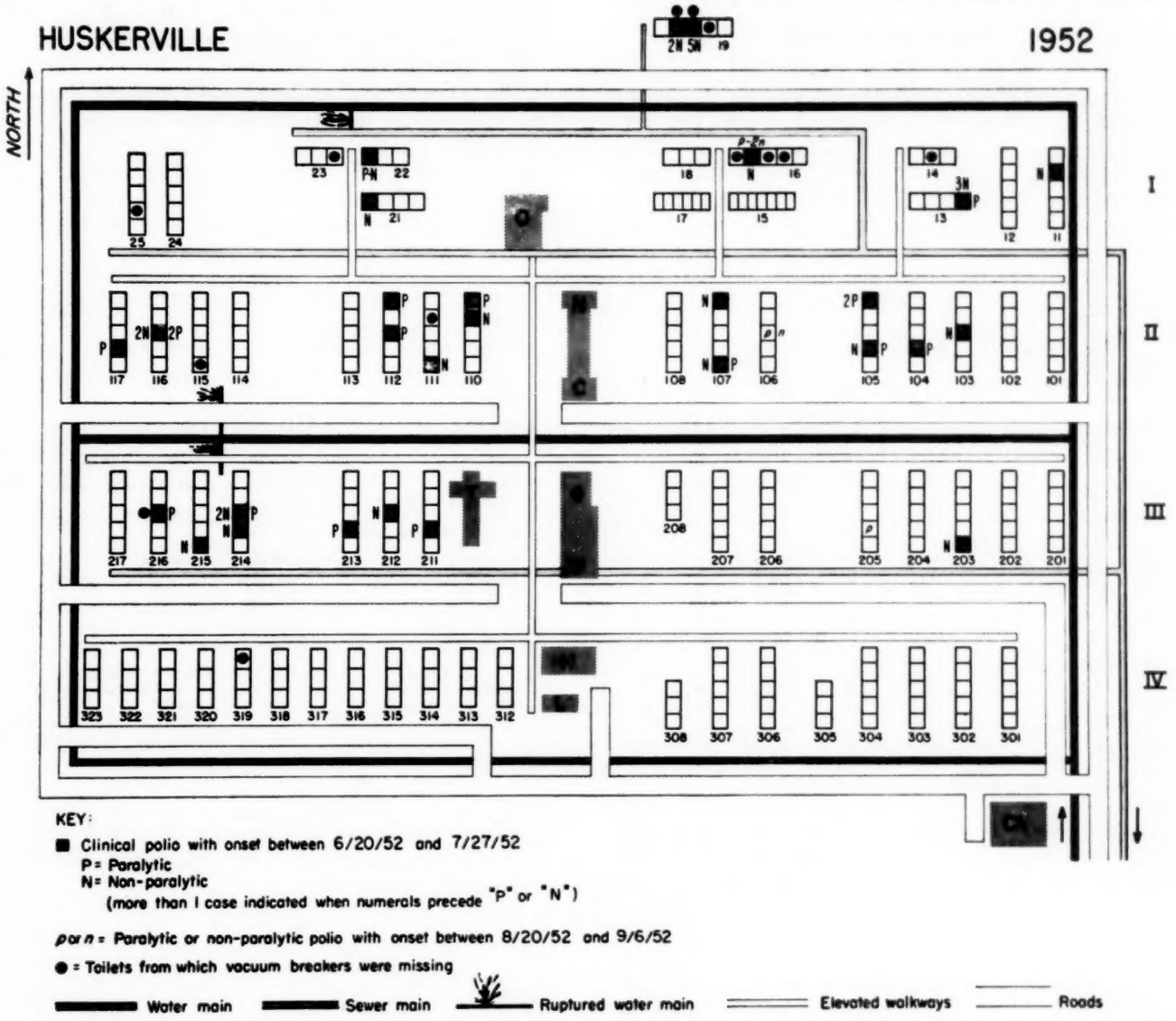


Fig. 1.—Map of Huskerville, a compact community of uniform dwellings, showing distribution of poliomyelitis cases in 1952, which were restricted almost entirely to rows I and II and the west half of row III.

The nearest stream was one mile away. Flowing through a straight artificial ditch, it was unattractive, inaccessible, and rarely visited by adults or children. A dry ravine on the north was unattractive and was not frequented. It was free of sewage.

Residents

The men of Huskerville, numbering 268, were veterans of World War II. They were a select group physically, intellectually, and emotionally. They had met the requirements for military induction. They had qualified for admission to the University of Nebraska. With the exception of one Oriental, they were all white. All were living on an income of from $2,000 to $3,000 a year, which was provided by the government and supplemented by the employment of one or both of the marital partners. All were married, and 98% of them had children.

The women of Huskerville numbered 271; 3 of them were widows with children. Wives of university students, they had been or were themselves university students. They were of better than average intelligence. They kept their simple homes remarkably clean and neat. There was none of the filth, disorder, crowding, or neglect that so often typifies low-cost housing areas. Although family incomes were low, the culture, as represented by family organization, sanitation, dietetics, and social customs, was definitely of the upper socioeconomic group.

The select character of the populace of Huskerville is most strikingly evident in the ages of its residents. Ninety-eight per cent were under 40 years of age, in contrast to the normal age distribution in Nebraska of

only 62% under 40 years. The ages of 80% of the men for whom ages were available were in the decade from 25 to 34 years inclusive. Of the women, the ages of 72% fell in the decade from 25 to 34 years and the ages of 92% in the period from 20 to 34 years.

There were 603 children. Most families had two or more children and families of from three to six were common. Of the children, 9% were in the first year of life, 60% under 5 years of age, and 92% under 10 years of age. The meager numbers of children in late childhood and of adults over 40 is strikingly apparent.

Movement of Adults

The men of Huskerville and a limited number of wives were students on the campus of the University of Nebraska. Some of the men and women had part-time employment in the city of Lincoln. These activities required a regular daily migration to the campus and metropolitan areas. Within the Huskerville area, adults, often accompanied by children, went to the central service area (fig. 1), which included the post office, drug store, soda fountain (D); day nursery (N); theater (T); club rooms, library, and doctors' office (C); rental office (O); launderette (L); and heating plant (H). There was a single church (Ch), in which services were held for Jews, Protestants, and Catholics. In a sociological study of Huskerville by a University of Nebraska graduate student, it was found that 97% patronized the grocer (G), 58% attended the theater, and the soda fountain was a very common meeting place. The central service area was not more than two city blocks from the farthest home. It was conveniently accessible by good, all-weather walkways. This central service area, of necessity, was frequented by one or more of every family in this compact community.

Movement of Children

Although the community was small and compact and was characterized by proximity and intimacy of social contacts, still the movement of children was restricted in several ways. Since 60% of the children were under 5 years of age and 92% were under 10 years of age, they generally were kept close to home. This was accomplished by enclosing the area between two barracks buildings to form a court. Since most of the buildings were built in pairs facing each other, the central court provided an enclosed area for the children from 6 to 10 family apartments. In this court from 10 to 40 children played in the greatest of intimacy. They shared a common sand pile and each other's toys. They could run in and out of their own or other apartments almost at will. The mothers, some working, some going to school, and all needing to make trips to market, took turns supervising these intimate "super family" court groups.

The movement of children was not limited only to the court; since the buildings were arranged in four rows (fig. 1), the elevated walkways, one of which extended the length of a row, served to limit the movement of children to traveling up and down a row. There was little cutting across between the rows. Access from one row to the other involved traveling to the central area and then crossing to the other row on the crosswalk.

In spite of the restrictions on the movement of children, it is true that children of all ages were frequently taken to the central service area. The community was typified by the frequency of contact and the absence of real geographical isolation or segregation for adults and children alike.

Incidence of Poliomyelitis and Other Illnesses in Huskerville in 1952

Clinical histories were secured on 1,049 persons, or 92% of the population of 1,142. Of this number, 577 (55%) denied having any illness during the summer of 1952. Of the 500 adults for whom records are available, 347 (70%) claimed to have been well. Of the 582 children, 230, or only 40%, were said to have been well through the summer of 1952. Approximately 60% of the children and 20% of the adults had an acute illness during the summer of 1952.

TABLE 1.—*Data on Twenty Patients in Huskerville Given Diagnoses of Frank Paralytic Poliomyelitis During 1952**

Week of Onset	Date of Onset	Case No.	Address†	Age Yr.	Age Mo.	Sex	Type of Poliomyelitis and Extent of Paralysis in 1952	Sequellae in 1955
Early Group								
6/22-28	6/24	1	213 D	3	4	M	Right arm and leg	Atrophy of deltoideus and gluteus muscles
	6/26	2	216 C	8		F	Bulbar‡	...
	6/27	3	13 D		10	F	Right leg	Flail leg
6/29-7/5	7/ 1	4	105 D	3		M	Right leg	Atrophy of gluteus and gastrocnemius muscles
	7/ 2	5	112 C	4		M	Right leg	Atrophy of gluteus muscles and hamstring
	7/ 4	6	117 D		5	M	Left leg	Atrophy of anterior tibialis muscles
	7/ 4	7	107 E	27		M	Right leg	Atrophy of quadriceps and gluteus muscles
	7/ 4	8	211 D	10		F	Neck and back	Scoliosis
7/6-12	7/ 6	9	110 A	7	7	F	Bulbar, leg	Atrophy of palate and leg muscles
	7/ 8	10	22 A	4		M	Bulbar, extremities‡	...
	7/ 8	11	211 C		11	F	Left leg	Flail leg, ½ in. short
	7/12	12	104 D	7		F	Right leg	Flail leg, contractures
7/13-19	7/16	13	112 A	2	4	F	Both arms and legs	Extensive atrophy of arms and legs
	7/18	14	105 A	1	6	F	Right leg	Flail leg
	7/18	15	105 A	3		F	Right arm and leg	Atrophy of deltoideus and gluteus muscles
7/20-26	7/22	16	116 C	3	3	F	Bulbar, face	Facial weakness, voice change
	7/24	17	116 C	27		F	Polioencephalitis	Atrophy of back muscles
Late Group								
	8/22	18	106 C	1	8	F	Arms and legs	Atrophy of anterior tibialis muscles
	8/27	19	16 B	30		F	Bulbar, left leg	Atrophy of anterior tibialis muscles
	9/ 6	20	205 D	4	6	F	Back and both legs	Scoliosis and flail leg

*A man, aged 32, who moved from Sioux City, Iowa, to Huskerville on May 15, when he was convalescent from the acute stage of paralytic poliomyelitis, is not counted. He lived in apartment 203B. All patients who had paralytic poliomyelitis were white.
† Numbers designate buildings, letters denote apartments in order from north to south.
‡ Patients died. Autopsy was done in case 2

Paralytic Poliomyelitis.—There were 20 cases (table 1) in 18 families (fig. 1) that were diagnosed as frank paralytic poliomyelitis. (These figures do not include the case of a 32-year-old man who moved into apartment 203B in May while he was convalescent from poliomyelitis acquired in Sioux City, Iowa.) In each of the 20 cases illness was acute, with fever, pain, muscle spasm, and paralysis. In each instance, diagnosis of paralytic poliomyelitis was made by the family physician and was confirmed by one or more consultants, usually pediatricians, internists, neurologists, or orthopedists. Either the patient in each case showed persistence of muscle atrophy or paralysis, often with a shortened or flail extremity, on reexamination in 1954 (two years later), or death had occurred during acute polioencephalitis, with abnormal spinal fluid and paralysis.

From the dates of onset listed in table 1, it is evident that a single severe outbreak occurred in the five-week period starting June 24. There was then an interval of approximately four weeks without new cases, and there was a final flurry of three cases in late August and early September. With the exception of the last case, all cases occurred in rows I and II and the west half of row III (fig. 1). This part of Huskerville, in which there was a high incidence of paralytic poliomyelitis, will be designated area A. Row IV and the east half of row III will be referred to as area B.

There were 347 children residing in area A. The 16 cases of paralytic illness among them constituted an attack rate of 4.6% among children in this part of the village. The severity of this epidemic is the more remarkable in view of the fact that only one case of paralytic poliomyelitis occurred among the 256 children and 211 adults residing in area B. From the statistical analyses presented in table 3, it is evident that the observed distribution of poliomyelitis would not be expected to result from chance alone.

Nonparalytic Poliomyelitis.—There were 31 cases (table 2) that we classified as nonparalytic poliomyelitis. They were found in 20 families, whose distribution is illustrated in figure 1. These were individuals with the symptoms of poliomyelitis, spinal or nuchal rigidity and transient weakness of limited muscle groups, but who presented no paralysis, weakness, or atrophy two years later. These individuals were usually, but not invariably, intimate household or "court" companions of those who had frank paralytic disease. It will be noted that the geographical distribution of the families coincides with the distribution of the families in which frank paralytic disease occurred. The statistical significance of these observations is summarized in table 3.

Of the 31 cases, the onset in 28 was between June 20 and July 27. Twenty-two of these cases were in children, and all of these children lived in area A. Adding this to the 15 children who developed paralytic poliomyelitis in June and July gives a total of 37, or an incidence of poliomyelitis (paralytic and nonparalytic) of more than 10% in a five-week period among children residing in this area. For the entire season, from June 20 through Sept. 6, there was a total of 16 paralytic and 24 nonparalytic cases among children. The total, 40, represents 11.5% of the children in this area. Among the children in area B, there were no cases of nonparalytic poliomyelitis.

Minor Illnesses.—There were 386 patients with minor illness in 111 families whom we classified as "poliomyelitis suspects." These illnesses were variously referred to by laymen and doctors as "summer flu," "summer diarrhea," "summer complaint," "flu," "summer colds," or "sore throat," and some were referred to by medical men as "virus disease of undetermined etiology," "virus X disease," "Coxsackie disease," "abortive polio," or "nonparalytic polio." Information about 449 adults and 514 children indicated that 23% of these adults and

TABLE 2.—*Data on Thirty-one Patients in Huskerville Given Diagnoses of Nonparalytic Poliomyelitis During 1952**

Week of Onset	Date of Onset	Case No.	Address	Age Yr.	Age Mo.	Sex
Early Group						
6/15-21	6/20	21	107 A	4		M
	6/20	22	110 B	5		M
	6/21	23	13 D	26		M
6/22-28	6/26	24	214 D	33		M
	6/27	25	13 D		27	M
	6/27	26	13 D		4	M
	6/28	27	19 B	7		M
	6/28	28	19 B	5		M
6/29-7/5	6/30	29†	16 B	3		F
	7/ 1	30	107 E	4		F
	7/ 1	31	212 C	8		M
7/6-12	7/ 6	32	214 C	2		F
	7/ 6	33	214 C	5		M
	7/ 6	34	215 E		11	F
	7/ 7	35	105 D		21	F
	7/ 8	36	19 C	5		M
	7/10	37	19 C	33		F
	7/10	38	19 C	13		M
	7/10	39	19 C	11		M
	7/10	40	22 A	2		M
7/13-19	7/15	41	11 B	4		F
	7/15	42	19 C	33		M
	7/15	43	21 A	35		M
	7/15	44	203 E	36		F
7/20-26	7/20	45	108 C	8		M
	7/24	46	116 C	5		F
	7/24	47	116 C	6		F
	7/27	48	111 E	10		M
Late Group						
8/17-23	8/20	49	106 C	26		F
	8/21	50†	16 B	9		M
	8/22	51†	16 B	7		M

* One adult residing in apartment 206 B was given a diagnosis of nonparalytic poliomyelitis, with the onset being on October 10. He was excluded in view of the long interval from the last previous case.

† The 3 children are siblings and children of the patient in case 19 (see table 1). After the patient in case 29 became ill, the other 2 children went to Chicago, where they remained through July and most of August. Their illnesses began on the train en route from Chicago to Huskerville.

TABLE 3.—*Chi-Square Analysis of the Distribution of Fifty-one Cases of Poliomyelitis in Huskerville in 1952*

	Type of Poliomyelitis*	Area A (High Incidence) Sick	Not Sick	Population	Area B (Low Incidence) Sick	Not Sick	Population	Total Population	Chi-Square	p
Children	P	16	331	347	1	255	256	603	9.5	0.002
Children	P and NP	40	307	347	1	255	256	603	29.0	0.00001
Adults and children	P	19	656	675	1	466	467	1,142	10.8	0.001
Adults and children	P and NP	49	626	675	2	465	467	1,142	30.0	0.00001

* P=paralytic; NP=nonparalytic.

55% of these children had a minor illness during the summer of 1952. The patients showed ill-defined illnesses, some of which were chiefly gastrointestinal, some respiratory, and others neuromuscular. Excluded from this group are such conditions as measles, rubella (German measles), roseola, chickenpox, mumps, scarlet fever, follicular tonsillitis, rheumatic fever, otitis media, traumatic conditions, and hysteria. Most of these people with ill-defined illnesses were suspected of having poliomyelitis at the time. Since serologic studies gave evidence that a high proportion of persons in the community were infected with poliomyelitis virus, it seems probable that many of these minor illnesses were associated with infection by this virus. However, available evidence does not permit a definite conclusion on this point.

Measles and Chickenpox.—In the spring of 1952, 114 children in Huskerville had red measles. In the fall of 1952, 85 children had chickenpox. The distribution of both measles (fig. 2) and chickenpox was random throughout the area. This constitutes evidence that there was no barrier to the ready dissemination of such diseases in the community. Furthermore, poliomyelitis spread through the community with greater intensity and greater rapidity and ran a shorter course than did measles and chickenpox.

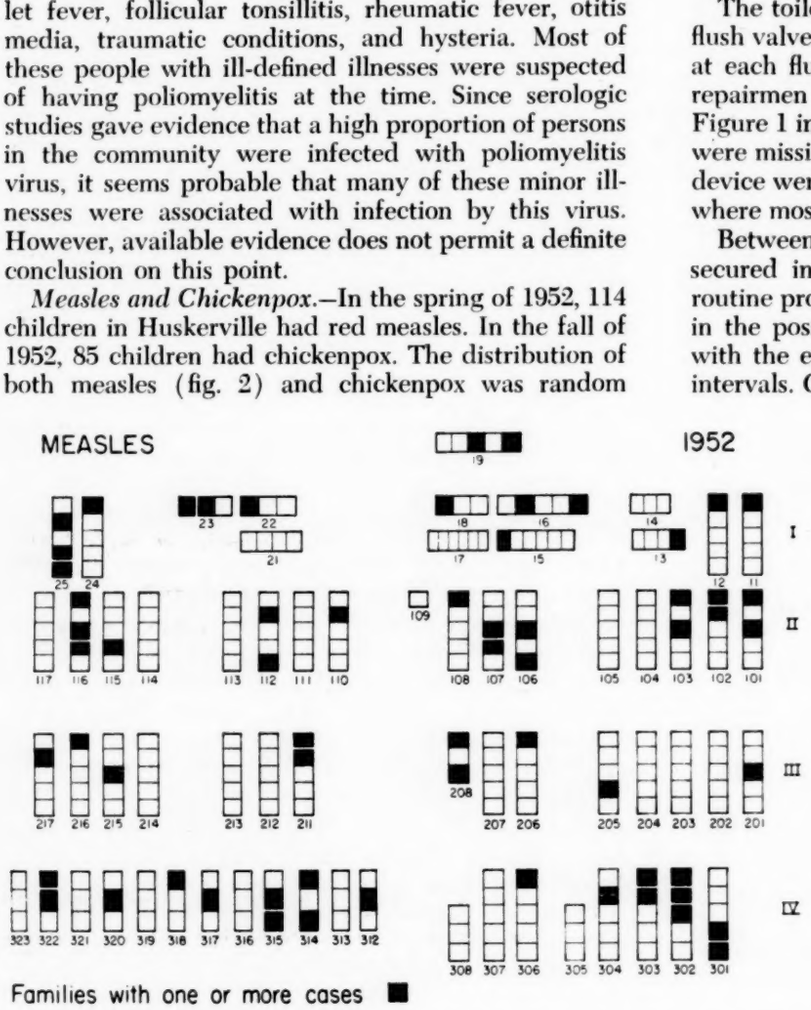


Fig. 2.—Map of Huskerville, showing that distribution of measles cases in 1952 was in a random pattern.

Water Supply and Sewage Disposal

The water supply of Huskerville was derived from the city of Lincoln, the source being deep wells. The water was chlorinated. It was carried through mains 8 miles in length, which entered Huskerville at the southeast corner (fig. 1). At this point the 8-in. main divided and encircled Huskerville in a terminal loop. There was a cross-connecting main traversing the area from east to west. Since this was a terminal loop, it is evident that the flow of water through both arms of the division gradually diminished in velocity until at some point in the distal portion of the loop the water became stagnant. The point at which there was no movement of the water fluctuated back and forth depending upon the use of water, particularly on unusual use of water from time to time.

The sewage system (fig. 1) was made up of two 8-in. sewers, which drained to the east and united to carry the sewage to the municipal sewage disposal plant.

The toilets throughout the area were equipped with flush valves. Originally vacuum breakers were installed at each flush valve, but in the course of recent years repairmen had removed some of these safety devices. Figure 1 indicates the sites where the vacuum breakers were missing; 12 of the 13 toilets that lacked the safety device were located in area A, the section of the village where most poliomyelitis cases occurred.

Between June 1 and Sept. 30, six samples of water secured in the boiler plant were tested. This was a routine procedure, and, at that time, no interest existed in the possibility of the water having anything to do with the epidemic. The tests were made at two-week intervals. Of these six samples only one showed a trace of chlorine. The bacterial counts ranged from 0 to 47. No lactose fermentation was demonstrated.

Failure of the Water System.—The growth of Lincoln in population and in industrial development prior to and throughout 1952 had been rapid. In this year an extensive program of construction was underway to expand the entire water system, which was rapidly becoming inadequate. A series of events occurred that threw an unexpected and unprecedented burden on the already overtaxed water system. The spring of 1952 was early, with unseasonably warm weather and good early rains. As a consequence, gardening and lawn work began several weeks earlier than usual, but by May 16, severe dry and hot weather led to drouth conditions, which were injurious to new lawns and gardens. Conditions became increasingly severe, and, for 17 days, from May 27 to June 12, there was no rain. The hottest heat wave and longest continuously dry spell for the month of June was recorded. The average temperature was 9 degrees above normal. Temperatures of 100 F or more were recorded on 10 different days during the month.

By June 12, a dangerous depletion of the water reservoirs occurred. Restriction of water was instituted. On June 14, in order to get water to the users at the periphery of the city (including Huskerville), the pressure in the heart of the city was dropped from a normal 70 lb. to 58 lb. per square inch and the outlying pumps were employed to boost pressure in the terminal mains.

At this critical time, on June 16, eight days before the onset of the epidemic, two breaks occurred in the large duct that brought water to the city of Lincoln. The loss of this main source of water left the city with a totally inadequate supply from small local wells and from depleted reservoirs.

June 18, a bakery only one mile from the main pumping station had to shut down because no water could be secured from its line. The larger industries had to

shut down in part or completely, and some used distilled water or cistern water to maintain partial operation.

Due to these conditions within the city of Lincoln itself, Huskerville at the terminus of the 8-mile water main suffered erratic pressure changes. This was aggravated greatly by developments at the nearby air base. As an initial step in a 41-million-dollar program of reconstruction for the decommissioned air base, the water mains in the air base area were at this time being repaired. It was found that two large mains that crossed under a small stream had been completely washed out by recent floods, many of the branch mains had been broken, and all had held stagnant water for several years. In order to clear the system, reduce bacterial counts, and establish a chlorine content acceptable to the military, extensive and repeated flushing of this system was employed. This heavy intermittent use of water at the nearby air base intensified the pressure fluctuations at the Huskerville area, creating occasions when there was insufficient water pressure to flush toilets and during which the engineer at the power plant found it necessary to utilize water from the hot water system to maintain the boilers of the heating plant. Since the outlying pump utilized to boost the pressure in this terminal main supplying the air base and Huskerville was at times uncontrolled, the engineer at Huskerville experienced great difficulty because of periods of excessive water pressure. At times, pressures of 125 lb. per square inch were reached in a system in which the normal pressure was from 35 to 40 lb. These periods of excessive pressure led to several ruptures in smaller water lines and to other mechanical failures, especially in the hot water system. A condition existed then in which the water system of Huskerville was subjected alternately to excessively high pressures, to very low pressures, and even to negative pressures.

Serologic Studies

Collection of Specimens and Laboratory Methods.—In May, 1954, serum was collected from almost all persons who resided in Huskerville at the time of the 1952 epidemic and were still living there. This number amounted to nearly half of the population at the time of the epidemic.

The serums were stored in the frozen state until they could be tested for neutralizing antibodies to poliomyelitis viruses. Most tests involved the use of HeLa cells essentially as described by Syverton, Scherer, and Elwood.[1] The technique of Salk, Youngner, and Ward,[2] based on observation of the pH of medium containing a suspension of monkey kidney cells, was also employed. Duplicate tests on more than 100 serums showed remarkably good agreement between results with these two methods. Poliomyelitis virus strains employed were the Mahoney strain of type 1, the MEF-1 strain of type 2, and the Saukett strain of type 3.

Neutralization of Poliomyelitis Viruses by Serums of Patients.—In interpretation of the results of serologic tests, neutralization by serum diluted 1:32 was accepted at evidence of previous infection. Neutralization by serum diluted 1:4 but not in higher dilution was regarded as a negative result. In the majority of negative tests, however, there was no neutralization of virus even at 1:4, and in most of the positive tests neutralization was present at dilutions higher than 1:32.

Studies of serums of patients who had clinical cases of poliomyelitis during the Huskerville epidemic of 1952 indicated that type 1 virus was responsible. The serums of all but 1 of these 16 patients tested were positive for antibody to type 1 virus. Of greater significance is the fact that seven of the patients with paralytic disease were children, the oldest being 4½ years of age. As is shown in table 4, the serums of all of these children were positive for antibody to type 1 virus. None had antibody to virus of type 2 or type 3. In the face of these results, it is safe to conclude that the epidemic of poliomyelitis in Huskerville must have been caused principally or entirely by type 1 virus. If types 2 or 3 were present in the community at the time of the epidemic, their distribution must have been limited, and they were not significant contributors to the high incidence of paralytic disease.

Results with Serums from Children in the General Population.—A major purpose of the serologic studies was to compare the extent of past infection among

TABLE 4.—*Data on Neutralization of Types 1, 2, and 3 Poliomyelitis Virus by Serums Collected in May, 1954, From Seven Patients Under Five Years of Age Who Had Paralytic Poliomyelitis During the 1952 Epidemic in Huskerville**

Case No.	Age at time of Epidemic, Yr.	Results with Type 1† Serum Dilution 1:4	1:32	1:128
4	3	++‡	++	++
11	11 mo.	++	++	++
13	2	++	++	++
15	3	++	++	++
16	3	A+	++	++
18	1½	++	+A	+A
20	4½	++	++	++

* Two tubes of monkey kidney tissue or HeLa cell culture were used for each test.

† Types 2 and 3 not neutralized in either tube by serums of any of the seven children at 3 dilutions tested.

‡ Code: ++ indicates virus was neutralized in both tubes; A indicates that cells in one tube showed atypical degenerative changes, and, therefore, this tube was disregarded in interpretation.

residents of that part of Huskerville where clinical poliomyelitis was common, area A, with that among residents of the section that was virtually free of clinical poliomyelitis during the epidemic, area B. Since it is known that in most communities in the United States only a small proportion of young children have antibodies to poliomyelitis virus, special attention was paid to tests of serums from children. The serums of 254 children, from 2 to 15 years of age, randomly distributed throughout the village were tested with type 1 virus, and the results are shown in table 5.

The data in table 5 present a pattern of antibody occurrence with respect to age that is remarkable in three respects: 1. The incidence of antibodies to type 1 virus is extraordinarily high in young children. The serums of 77% of those under 5 years of age were positive. 2. There is no increase in antibody incidence with age. The incidence of antibodies in children of preschool age is equal to that in older children. 3. There is a consistent pattern of moderately higher incidence of antibodies to type 1 virus among residents of area A than among residents of area B

in the various age groups. It is not profitable to compare the incidence of antibodies in the smaller groupings of buildings within areas A or B, since the differences were not significant and were well within the range to be expected from random sampling.

A limited number of serums have been tested for the presence of types neutralizing antibodies to types 2 and 3. The serums were selected to insure representative distribution within the village. Of 39 serums tested, 6 (17%) showed evidence of past infection with type 2 virus, and 5 (23%) of 22 serums tested were positive for antibodies to type 3 virus. There was evidence of increasing incidence of antibodies with age.

As the serologic tests progressed and the remarkably high incidence of antibodies to type 1 was noted, it was decided that similar tests on serums from children who moved to Huskerville after the epidemic of 1952 might be helpful in the interpretation of these data. Therefore, serums from children 1½ to 6 years of age

TABLE 5.—*Age Distribution of Children Who Lived in Huskerville During 1952 Epidemic Whose Serums Were Tested With Type 1 Poliomyelitis Virus in 1954**

	Reactions in Serums†			
	Residents of Area A (High Incidence)		Residents of Area B (Low Incidence)	
Age, Yr.	Negative, No.	Positive, No.	Negative, No.	Positive, No.
2	2	9	2	4
3	4	16	6	6
4	1	13	4	9
5	3	17	3	9
Total	10	55(85%)	15	28(65%)
6	3	18	7	4
7	4	13	8	10
8	2	2	2	8
9	3	13	1	4
10	0	3	3	6
11-15	1	19	5	7
Total	13	68(84%)	26	39(60%)

* Among the children are 35 who had paralytic and nonparalytic poliomyelitis in 1952, all of whom were positive for neutralizing antibodies and were residents of area A.

† All serums considered positive neutralized virus in a dilution of at least 1:32. Those considered negative either showed no neutralization or were positive in a dilution no higher than 1:4.

who moved into Huskerville after the epidemic of 1952 were collected in July, 1955. Of the 17 serums tested, 5 (29%) showed neutralizing antibodies to type 1 virus. Only one child had antibodies to type 2. Four, or 24%, had antibodies to type 3 virus. Presumably some of those found to have antibodies in 1955 may have been infected in 1952 and resided in other epidemic areas at that time.

Analysis of Distribution of Cases and Possible Causes of Epidemic

The relatively large population of children, 60% of whom were less than 5 years old, is of great advantage in analyzing this epidemic. It may be assumed that many of the adults were immune to poliomyelitis before 1952. However, the number of children who were immune before the epidemic must have been very small. The incidence of disease among the children is, therefore, the most meaningful measure of the extent of the epidemic.

According to the data shown in table 3, there is only 1 chance in 500 that the observed distribution of paralytic cases between the populations of children in areas A and B would occur due to chance alone. If one includes both paralytic and nonparalytic cases, the likelihood that chance alone can account for the observed distribution is only 1 in 100,000. There is unquestionably strong reason for seeking a reason, other than the chance distribution of cases, for the high incidence of clinical poliomyelitis in the two and one-half rows of dwellings that comprised area A.

The primary purpose of this study was to evaluate factors that might account for the remarkable difference between the numbers of poliomyelitis cases in the parts of the village, which we designate as area A and area B. It seemed highly probable that some environmental influence was operative either in protecting the residents of area B or in enhancing the severity of the epidemic in area A. All ordinary personal characteristics, such as genetic constitution, personal cleanliness, or past exposure to disease, could be eliminated from consideration, for the residents of area A and area B were randomly distributed with respect to such factors.

Pregnancy, overexertion, drastic changes in temperature, surgical trauma, infections, immunizing procedures, and other conditions have been implicated as influencing the course of infection in individuals and in small groups. However, such factors cannot account for the distribution of paralytic disease in Huskerville. The distribution of pregnant women was in no way related to the distribution of cases. Neither physical exertion nor trauma could be related to any localized picnic or sporting competition, for there was no event, attendance at which was restricted to any portion of the populace. There was one large picnic, involving the families of the men in the university Naval Reserve unit, that took them to a nearby resort where swimming and outdoor games were participated in, but these families were drawn from all parts of Huskerville.

Environmental Factors Possibly Influencing Spread of Poliomyelitis.—Efforts were made to find environmental factors that might have a broad impact upon the community. Meteorological conditions in this small area were remarkably uniform and presented no apparent explanation for the restricted distribution of paralytic disease. There were no open privies and no sewage-polluted streams in the area. No wild animals, domestic animals, or vermin were found except as they affected all parts of the area.

Mosquitoes: One infant who developed severe paralytic disease had been badly bitten by mosquitoes. The early, warm spring with generous rains brought mosquitoes out earlier than usual and in abundance. In retrospect, it does not seem likely that mosquitoes were appreciably more numerous in either the north, which was nearest the dry creek bed, or in the east, toward which drainage from the area ran. Mosquitoes were numerous throughout the area.

Food: The food eaten in the area was derived from the single central grocery store or brought out from the distant metropolitan area. It was impossible to show

that the source of foods differed in any one part of the community as compared with another. Pasteurized milk was used throughout the area by all but eight families. The milk was distributed by eight different firms. There were no milk routes that could in any way be related to the epidemic.

Gardens: There were a number of garden plots on the east side of the area where fresh vegetables were grown for the table. These gardens were watered with water from the municipal water supply. There was no apparent sewage contamination of these gardens. They were planted and the fresh vegetables were largely consumed by the residents on the east side of Huskerville, the area in which the disease was less prevalent.

Presence of Flora: Susceptibility to bacterial infection of the alimentary tract may be greatly influenced by the normal flora.[3] It is quite possible that initiation of poliomyelitis infection in the pharynx and/or intestine may be similarly influenced by the numbers and kinds of bacteria and viruses present on the mucosal surfaces in these areas of the body. The composition of the normal flora is of variable character, and presumably there might have been some organism more prevalent in the throats or intestines of Huskerville residents in one part of the community than in those of residents in another area. For the present, it is sufficient to state that there is no direct evidence for or against the influence of normal flora on the Huskerville epidemic.

Water: Water supplies have long been regarded with suspicion as possible means of dissemination of the poliomyelitis virus, largely because of the remarkable parallelism between poliomyelitis and the enteric fevers. Some of the pertinent evidence is the occurrence of poliomyelitis in the summer months; the presence of virus in abundance in sewage; the viability of virus in water, milk, and milk products for many weeks; and the fact that the disease can be produced in suitable animals by the ingestion of food contaminated with virus.

It is evident from the meager water testing that was done during 1952 that we know little about the water that the residents of Huskerville were drinking at the time. The few samples tested were taken at two-week intervals. Much pollution could have occurred in an interval of 14 days that, by chance, would not appear in the tests. Furthermore, the tests were taken at a single site, the power plant. The power plant draws its water directly from the water main near the point where it enters Huskerville. Water from a point located near the inlet would be least apt to show contamination originating in the community. The importance of the site at which water was collected was clearly demonstrated in 1954, when water samples were taken at three different locations. During the month of July, 10 samples of water secured at the power plant were tested, and they were found to show bacterial counts of zero. On the other hand, of 10 such samples taken at the drug store, 4 had bacterial numbers too great to be counted and 4 had counts of 80, 10, 10, and 10 respectively. Only two tests taken at this site were reported as showing bacterial counts of zero. At the rental office in this same period, the bacterial counts were rather erratic, ranging from 0 to 100. It is evident that the boiler house, near the intake, had the cleanest water. It is also evident that the test sites in rows II and III had higher bacterial counts. There was no known deterioration in the water system between 1952 and 1954 that would give reason for us to believe that the water was less subject to contamination in 1952 than in 1954. Unfortunately, at no time before or since have samples been tested in the most distal portion of the water loop, where bacterial counts would be expected to be highest.

Although none of the 16 water samples tested during the entire year 1952 showed the presence of bacteria of the coli-aerogenes group, it is noteworthy that 2 samples out of 10 examined in 1951 were found to contain such fecal organisms.

It may be concluded that the meager testing that was done in 1952 has very little value in this study, except to establish the fact that there was insufficient chlorine in the water to have any effect upon virus contamination. The high bacterial counts on later tests and the recovery of coliform bacteria on two occasions in 1951 strongly suggest that fecal contamination may have occurred within Huskerville in 1952. This possibility is supported by other evidence.

So long as full pressure was maintained in the mains, the influx of pollution would be impossible; but, since the reservoir located on a hill near by, which had been a part of the original installation, had been cut out of the system, any break in the line, failure of the pumps, or unusual use of water at any point along the 8-mile line, because of the incompressibility of water and the inelasticity of the mains, would immediately be reflected in a fall in pressure in Huskerville. Such events did occur. There was unprecedented water use due to growth of the city and drouth conditions. A break in one of the principal water mains in Lincoln eight days before the epidemic started led to a severe impairment of the water service. Heavy intermittent use of water to flush out contaminated mains at the nearby air base and the rupture of several local mains in Huskerville itself caused numerous episodes of lowered pressure. Since the northwest portion of the loop was the most distant as well as the highest point in the system, the greatest pressure drop would occur there and negative pressure would occur there first and most frequently.

In older toilets and in many modern toilets a water tank is employed to produce the pressure for flushing. This arrangement provides a complete break between the potable water source and the water in the toilet bowl. This is the safest system. In public buildings and in increasing numbers of private homes, toilet installations have been employed that do not have a water reservoir. In these units the pressure in the water main is used for flushing, and a direct connection exists at this time between the potable water source and the toilet bowl. So long as positive pressure is maintained in the water main, no hazard exists, but, if there is a failure of the water pressure and negative pressure develops in the main, then air and water will be siphoned back into the main from the toilet bowl—if the flush valve at the time is opened as in flushing or if the flush valve is closed but incompetent.[4] If a toilet

is clogged and the bowl filled to the brim, as was observed in the central area on several occasions during the summer of 1952, then soiled water may be readily siphoned back, but, even in an unblocked toilet, sufficient negative pressure can aspirate soiled water from the bottom of the bowl.

This great hazard to our drinking water has received much attention in the literature of the sanitary engineering profession, but it has been infrequently recognized in the medical literature. Because of the gravity of this problem the sanitary code of Lincoln makes flush valve toilets illegal unless a safety device, a vacuum breaker, is installed between the flush valve and the toilet bowl. This device admits air into the inlet pipe in the event of negative pressure and prevents siphonage from the toilet bowl.

Since the height of the toilets at the west edge of Huskerville was 25 ft. above those at the east border, if the pressure in the system dropped to zero at the inlet, the negative pressure exerted on the flush valves would range from 10½ lb. to the square inch, that of a column of water 25 ft. in height, on the west to zero on the east. If the pressure drop was less, producing zero pressure at a midpoint (this was observed at the power plant), then negative pressure at the west border would be about 5 lb. to the square inch and positive pressures would exist east of the point. During repair of three breaks in the water mains within Huskerville, the flush valves of the distal portion of the water main loop were necessarily subjected to negative pressures.

It is a remarkable coincidence that 12 of the 13 toilets without vacuum breakers were in the area of high poliomyelitis incidence and that clinical poliomyelitis did not occur during the epidemic in row IV or in the east half of row III, which were closest to the water intake for the area, had safe toilets, had no water main breaks, had the least fluctuation of water pressures, and had the lowest bacterial counts. This combination of facts points to fecal pollution of the water supply close to the point of water utilization as a factor that may have been responsible for the high incidence of clinical poliomyelitis in area A.

The principal evidence against the idea that proximate fecal pollution was causally related to the high incidence of poliomyelitis in area A is found in a comparison of data from the east half of row II with that from the east half of row III. These two rows of buildings derived their water from the same stretch of the main that ran between them, yet there were five paralytic and four nonparalytic cases among 68 children in this part of row II and only one paralytic and no nonparalytic cases among 77 children in the corresponding part of row III. The likelihood that this difference would occur due to chance alone is approximately 1 in 6, if one considers only paralytic cases, and 1 in 100, if one considers both paralytic and nonparalytic cases.

Stratification in the flow of fluid through a pipe is well known to occur and might have caused uneven distribution of polluted water in this area. It would be of interest to know whether there was a slight difference in the elevation of the branching pipes leading from the two sides of the pipe. If those on the north side were slightly depressed, polluted water might drain preferentially in that direction, since the pollution presumably occurred when there was negative water pressure.

Despite explanations, such as these, that may be marshalled to account for the differences in the east half of rows II and III, these differences are good reason for maintaining an attitude of reserve relative to the proposed explanation for the high incidence of poliomyelitis in area A of Huskerville. Proximate fecal pollution of the water supply is the only potentially significant environmental factor that has been discovered. Intrinsic factors, such as those of a physiological or genetic character, can be ruled out since they would occur in random distribution in the community. The bacterial flora of the respiratory tract and alimentary canal in different individuals would vary in a nonrandom fashion and might conceivably be related to the pathogenesis of poliomyelitis, as was suggested by Ingalls and Aycock.[5] However, this latter explanation appears more tenuous than the hypothesis that proximate fecal pollution was the important factor.

Possible Factors Influencing Severity of Case of Poliomyelitis.—If, as a working hypothesis, it is accepted that fecal pollution of water from nearby defective toilets was in some way causally related to the high incidence of clinical poliomyelitis in area A, then it becomes important to ascertain whether spread of virus was restricted to the areas in which a high incidence of clinical disease occurred. The crucial question becomes: Did proximate fecal pollution influence primarily the severity of infection, or did it merely determine the distribution of infection?

The widespread occurrence of minor illnesses among residents of both area A and B suggested to clinical observers that infection by poliomyelitis virus was prevalent throughout the village, even though infections meeting the criteria for diagnosis as paralytic and nonparalytic poliomyelitis were largely restricted to area A. Serologic studies bearing on this point have been presented. The results summarized in tables 4 and 5 provide adequate evidence to conclude with confidence that type 1 poliomyelitis virus was the cause of the epidemic. The role played by types 2 and 3 must have been negligible. No other interpretation is reasonable in view of the findings in tests of serums from patients with paralytic disease. Likewise, the tests for antibody in children under 6 years of age can lead only to the conclusion that type 1 poliomyelitis virus had been remarkably prevalent, whereas types 2 and 3 had not been prevalent to any unusual degree in the community in the previous two years. Since there is good evidence that antibodies to the poliomyelitis viruses persist for many years,[6] the fact that serum was collected in May, 1954, whereas the epidemic occurred in the summer of 1952, does not interfere seriously with this interpretation.

Comparison of the incidence of antibodies to type 1 virus in areas A and B leads to two interesting conclusions: 1. The incidence of past infection with type 1 virus was approximately one-fourth less in area B than in area A. 2. The incidence of neurological involvement, with or without permanent paralysis, was higher among infected persons in area A than among those in area B. Data supporting this conclusion are presented in table 6.

There were 347 children residing in area A and 256 children residing in area B at the time of the epidemic. If, for reasoning purposes, we estimate that the infection rate during the epidemic was 80% for children residing in area A and 60% for children in area B, then it follows that the number of children infected was approximately 278 in area A and 154 in area B. The number of children who developed poliomyelitis with signs of meningeal irritation (paralytic and nonparalytic cases) was 40 in area A; 16 cases were paralytic. This is a total attack rate of 14% among the infected children and an attack rate for paralytic poliomyelitis of 5.8%. If there had been a similar attack rate among infected children in area B, there would have been 22 cases, including 9 paralytic cases. There was one paralytic case, and there were no nonparalytic cases.

In table 3 it is shown that the probability that chance alone could account for the observed distribution of poliomyelitis cases in areas A and B was very small. In estimates of probability, values of p ranged from 0.001 to 0.00001, depending upon the type of analysis made. In table 6, the results of similar calculations are presented with adjustment for the fact that the infection rate was somewhat lower in area B than in area A. The results show again that chance distribution is a highly unlikely explanation for the fact that more cases of clinical poliomyelitis occurred in area A than in area B. In fact, if one considers both paralytic and nonparalytic cases, the probability of the observed result occurring as a result of chance alone is approximately 1 in 100,000. It is difficult to escape the conclusion that some environmental factor caused an increase in the incidence of clinically significant neurological involvement among those infected with type 1 poliomyelitis virus in area A. Proximate fecal pollution is the only environmental feature to which it seems reasonable to ascribe this significance. The data in table 5, showing a high rate of past infection among children in area B, support the concept that, relatively speaking, there is a safe way and a dangerous way to be infected with poliomyelitis virus and that at least some of the Huskerville children in area A acquired virus by the dangerous way whereas in area B infection was predominantly by the "safe" way.

Lepine [7] has suggested that the mode of transfer of poliomyelitis virus may be important in determining whether paralytic disease results from infection. His suggestion was that clinical disease may be enhanced by direct contamination from human to human via the respiratory tract, whereas indirect contamination via the digestive tract may be responsible for the commonly occurring immunization. He also referred to the possible importance of the quantity of virus introduced during infection.

The fundamental concept that route of transfer of virus may be of special significance deserves careful consideration in future epidemiologic studies. It is too early to attempt generalizations regarding the significance of specific routes. In the case of the Huskerville epidemic, however, the evidence points strongly to ingestion of water obtained close to the point at which pollution occurred as one kind of viral transfer that was especially dangerous.

There appear to be three possible mechanisms by which proximate fecal pollution of water might increase the severity of infections with poliomyelitis virus: 1. The effect might be quantitative and depend upon the amount of virus taken in at the time of infection. Proximate fecal pollution of water might lead to ingestion of relatively large amounts of virus, amounts that increase the frequency of invasion of the central nervous system. 2. The anatomic site or sites of primary infection may be different, if infection results from ingestion of poliomyelitis virus in water, from the sites of primary infection if virus is acquired by other means. For example, it is possible that primary infection in both the pharynx and the ileum is common after ingestion of virus in water but that initial infection is limited to the pharynx if virus is inhaled in droplets. If the site of initial infection is the significant factor, it must also be true that some site or sites infected by virus in water are more favorable for the subsequent invasion of the central nervous system than are those infected by other routes. 3. A third possible mechanism that might be influenced by proximate fecal pollution of water relates to the normal flora, microbial and viral, of the alimentary tract. It is possible that drinking polluted water led to establishment of

TABLE 6.—*Estimates of Attack Rates of Clinical Poliomyelitis Among Infected Children in Area A (High Incidence) and Area B (Low Incidence) in Huskerville in 1952*

			Cases of Poliomyelitis			
			Paralytic and Nonparalytic		Paralytic	
Population of Children	Estimated No. Infected		No. of Cases	% of No. Infected	No. of Cases	% of No. Infected
Area A 347	278	(80% of total)	40	14.39	16	5.76
Area B 256	154	(60% of total)	1	0.65	1	0.65
Difference between area A and area B			Chi-Square=20.6; p=0.00001		Chi-Square=6.8; p=0.009	

one or more significant organisms in the alimentary tracts of some persons in area A. Secondary effects on other competitive organisms in the alimentary tract may also have occurred. It is conceivable that these changes in turn led to conditions more favorable for invasion of the central nervous system by poliomyelitis virus.

Implications of Findings with Respect to the Prevention of Poliomyelitis.—A good review of past observations and current opinions concerning the spread of poliomyelitis virus by water is presented by Gear.[8] For many years Kling [9] has been the leading exponent of the importance of this mode of spread. The principal argument against regarding spread by water as an important factor in the epidemiology of poliomyelitis is that noted by Maxcy [10]: "There is no instance on record up to the present in which convincing evidence has been presented that pollution of a community water supply was responsible for indirect and widespread exposure of consumers to infection with the virus."

We subscribe to the validity of this argument. If, however, paralytic infection derived from water is contingent upon pollution of the water supply close to the person to be infected, as appears to have been the case in Huskerville, then the role of water in the epidemiology of poliomyelitis must be reexamined. In-

stitutional epidemics or the clustering of cases in certain buildings, or even in certain parts of buildings, or in certain small villages, might be explainable if proximate pollution of water is an important factor. Future outbreaks should be studied with a view to determining the significance of this factor.

It appears that, in some other instances, as in Huskerville, drinking water judged to be safe by ordinary good standards of treatment and surveillance may be a significant source of clinical poliomyelitis. The boiling of drinking water during epidemic periods constitutes a simple technique immediately available and capable of wide application in communities in which the possibility of infection from this source cannot be ruled out. The concept of proximate pollution occurring in the distribution system, rather than community-wide pollution, should be stressed.

Comment

Chance distribution of cases is an unlikely explanation for the low incidence of frank poliomyelitis in one section of Huskerville at a time when a severe epidemic prevailed in the remainder of the community. There is good reason to conclude that there was fecal pollution of water proximate to the places of residence of persons who developed paralytic or nonparalytic poliomyelitis. No other sociological or environmental factor shows any correlation with the distribution of poliomyelitis cases. It is suggested that proximate fecal pollution may have been responsible for a somewhat higher infection rate in the area of high incidence of clinical disease. This alone cannot explain the difference in incidences of clinical disease in the two areas. Therefore, it is further suggested that proximate fecal pollution also was responsible for the greater severity of the infection in certain persons in area A.

Three possible mechanisms whereby proximate fecal pollution might influence the severity of infection are suggested: 1. The incidence of neural involvement may be greater as a result of larger infecting doses of virus, associated with proximate fecal pollution. 2. The site of primary infection may be different and more favorable for invasion of the central nervous system if virus is ingested in water than, for example, if it is taken in as droplets. 3. An alteration of the microbial or viral flora of the alimentary tract as a result of ingestion of polluted water may be conducive to invasion of the central nervous system when poliomyelitic infection supervenes. This last is regarded as the least probable of the three mechanisms. The first two are considered as not being mutually exclusive, and both may be operative. In view of the serologic evidence that the infection rate with poliomyelitis virus of type 1 was high in the area in which no paralytic cases occurred, it is suggested that the virus may have spread in a different and less dangerous way in this part of the community than in the area where many cases occurred. In other words, it is proposed that there may be a relatively safe way to contract poliomyelitis virus and a relatively dangerous way to receive the virus.

Until the significance of proximate pollution of water in the epidemiology of poliomyelitis can be assessed further, the boiling of drinking water in the home is a measure that should be considered as one precaution of possible value in prevention of the disease in times of epidemic. In considering whether to make such a recommendation, it is pertinent to recall the well-known fact that cross connections and other conditions favoring fecal contamination of water supplies are still common in water distribution systems.

Summary

In 1952 a severe epidemic of poliomyelitis occurred in Huskerville, a community of University of Nebraska students and their families near Lincoln, Neb. All but two cases, one paralytic and one nonparalytic, occurred in two and one-half of the four rows of barracks-like buildings. The 16 paralytic cases among 347 children residing in the two and one-half rows in the village constitute an attack rate of 4.6%. Fifteen of these developed within a period of five weeks. Reasons for the relative absence of clinical disease in the one and one-half rows of buildings, with a population of 211 adults and 256 children, were sought.

There were no geographical or social barriers nor any biological or other environmental factors that correlated with the distribution of cases. Measles and chickenpox spread in the same community without any higher incidence occurring in particular areas.

A variety of evidence pointed to proximate fecal pollution of the water supply as the sole factor to which significance could be attributed in explaining the distribution of clinical poliomyelitis within the community. The evidence indicating probable fecal pollution of water in the area where disease occurred was indirect but substantial. It concerned the presence of 12 toilets lacking vacuum breakers, which would prevent aspiration of soiled material into the water system in the area of high poliomyelitis incidence; the occurrence of many episodes of low pressure and negative pressure in the Huskerville water mains, these episodes being most marked in the general area of high poliomyelitis incidence, due to the slope of the land; the absence of protective amounts of chlorine in the water; and, at a later date, the demonstration of the presence of coliform organisms in the water in the part of the village where poliomyelitis cases occurred more frequently.

Tests for neutralizing antibodies were made with serum collected in May, 1954. Of seven children 4½ years old or younger who had paralytic disease in 1952, all had antibodies to type 1 virus and none had antibodies to viruses of type 2 or 3. Of 108 serum specimens from children who resided in 1952 in the section of the village that was almost free of clinical poliomyelitis, 62% had antibodies to type 1 virus. Of 146 children who resided in the area in which paralytic and nonparalytic disease had a high incidence, 84% had antibodies to type 1 virus. There was no increase in the frequency of antibodies according to the ages (from 2 to 15 years) of the children.

1431 S. 33rd St. (2) (Dr. Bancroft).

Dr. Velma C. Chambers assisted with the serologic tests for this study.

Viruses used in the serologic studies were supplied as infected-tissue-culture fluid in the frozen state by Connaught Medical Research Laboratories, Toronto, Canada, as part of the vaccine evaluation program sponsored by the National Foundation for Infantile Paralysis in 1954.

This investigation was supported in part by a research grant from the National Institutes of Allergy and Infectious Diseases of the National Institutes of Health, U. S. Public Health Service, and by grants from the University of Nebraska Research Council, the Cooper Foundation, Lincoln Optomists Club, and the Lincoln Junior League.

References

1. Syverton, J. T.; Scherer, W. F.; and Elwood, P. M.: Studies on Propagation in Vitro of Poliomyelitis Viruses: V. Application of Strain HeLa Human Epithelial Cells for Isolation and Typing, J. Lab. & Clin. Med. **43:**286-302 (Feb.) 1954.

2. Salk, J. E.; Youngner, J. S.; and Ward, E. N.: Use of Color Change of Phenol Red as Indicator in Titrating Poliomyelitis Virus or its Antibody in Tissue-Culture System, Am. J. Hyg. **60:**214-230 (Sept.) 1954.

3. Bohnhoff, M.; Drake, B. L.; and Miller, C. P.: Effect of Streptomycin on Susceptibility of Intestinal Tract to Experimental Salmonella Infection, Proc. Soc. Exper. Biol. & Med. **86:**132-137 (May) 1954.

4. Dawson, F. M., and Kalinske, A. A.: Report on Plumbing Cross-Connections and Back-Siphonage Research, Technical Bulletin of National Association of Master Plumbers of United States, Inc., Washington, D. C., 1938.

5. Ingalls, T. H., and Aycock, W. L.: Upper-Respiratory Infection as Factor in Influencing Susceptibility to Poliomyelitis, New England J. Med. **245:**197-203 (Aug. 9) 1951.

6. Miller, C. A., and Wenner, H. A.: Antibody Responses to Naturally Occurring Poliomyelitis Infections in Children: I. Neutralizing Antibodies Against the Prototype and Patient's Own Viruses, Pediatrics **14:**573-584 (Dec.) 1954.

7. Lepine, P.: Epidemiology and Pathogenesis of Poliomyelitis: Present Status of Problem, in Poliomyelitis: Papers and Discussions Presented at the Third International Poliomyelitis Conference, Philadelphia, J. B. Lippincott Company, 1955, pp. 129-136.

8. Gear, J. H. S.: Extrahuman Sources of Poliomyelitis, in Poliomyelitis: Papers and Discussions Presented at the Second International Poliomyelitis Conference, Philadelphia, J. B. Lippincott Company, 1953, pp. 343-354.

9. Kling, C.: Le rôle des eaux d'égout comme disséminateur du virus poliomyélitique, Presse méd. **55:**848-849 (Dec. 20) 1947.

10. Maxcy, K. F., quoted by Gear,[8] pp. 345-346.

VENTRICULAR SEPTAL DEFECTS

THEIR NATURAL TRANSFORMATION INTO THOSE WITH INFUNDIBULAR STENOSIS OR INTO THE CYANOTIC OR NONCYANOTIC TYPE OF TETRALOGY OF FALLOT

Benjamin M. Gasul, M.D., Robert F. Dillon, M.D., Vlastimil Vrla, M.D.
and
Gershon Hait, M.D., Chicago

• The natural course of patients with ventricular septal defects is not known. During the past 10 years, 27 autopsies were performed on the authors' 336 patients with this defect. Twenty-six of these patients were under 6 months of age. It has been observed repeatedly that some infants with large ventricular septal defects manifest marked improvement in their symptomatology after their first year of life. In an attempt to explain these observations, clinical follow-up examinations were combined with cardiac recatheterization and angiocardiography, especially on those patients who had their initial studies during their first year of life. So far, 10 patients have been restudied and recatheterized. The time interval between their first cardiac catheterization and the recent ones varied from three to five years. Two of these patients now present typical clinical and hemodynamic data of ventricular septal defect with infundibular stenosis with left-to-right shunts. The third patient shows typical findings of tetralogy of Fallot with marked cyanosis and predominant right-to-left shunt. The frequency with which this natural transformation of ventricular septal defects into apparently different entities occurs is at present not known. The concept of the unity of origin of the three entities has been demonstrated in these patients, and this concept should lead to a re-evaluation of our knowledge concerning the diagnosis and medical and surgical treatment of congenital cardiac defects.

This is a preliminary report on our studies of patients with ventricular septal defects. The purpose of this paper is to introduce a new concept of the course of ventricular septal defects in some patients. Our early studies, based on clinical, roentgenographic, electrocardiographic, and angiocardiographic findings and data on repeated cardiac catheterization, indicate that in some patients with ventricular septal defects this isolated malformation may be transformed into a ventricular septal defect with pulmonary stenosis or into a cyanotic or noncyanotic type of tetralogy of Fallot. The availability of open cardiac surgery for patients with ventricular septal defect makes additional and, particularly, new information regarding an alternate transformation of this defect extremely pertinent.

Method of Investigation

Since the establishment of the pediatric cardiophysiology department of the Cook County Children's Hospital in 1947, we have observed 336 patients with ventricular septal defects. While most of these patients came from the Cook County Children's Hospital, a number of them were transferred from the Research and Educational Hospitals of the University of Illinois College of Medicine and from the Presbyterian Hospital. In 83 of these patients cardiac catheterization was performed, and in 85 angiocardiograms were taken. Operations were performed on only two patients. In the process of evaluating the natural course of this malformation by means of repeated clinical examinations and laboratory studies, we found that a number of patients who had previously had a loud,

From the Hektoen Institute for Medical Research, the Cardiophysiology Department of Cook County Children's Hospital, and the departments of pediatrics of the University of Illinois College of Medicine and Presbyterian Hospital.

Read before the Society for Pediatric Research, Carmel, Calif., June 17, 1957.

booming second sound over the pulmonary area, a sign of high pressure in the pulmonary circuit, presented on subsequent reexaminations a definitely diminished second sound over this same area. As a result, we decided to recatheterize some of these patients, particularly those who had had cardiac catheterization performed either in infancy or, at least, a number of years previously. At this very early stage in our studies, we were impressed by the observation that, of three patients who had first undergone cardiac catheterization during the first year of life, one showed evidence of having a ventricular septal defect, with a definitely localized infundibular stenosis, and another showed findings indicating so-called noncyanotic type of tetralogy of Fallot. The third patient still manifested findings of only a large ventricular septal defect.

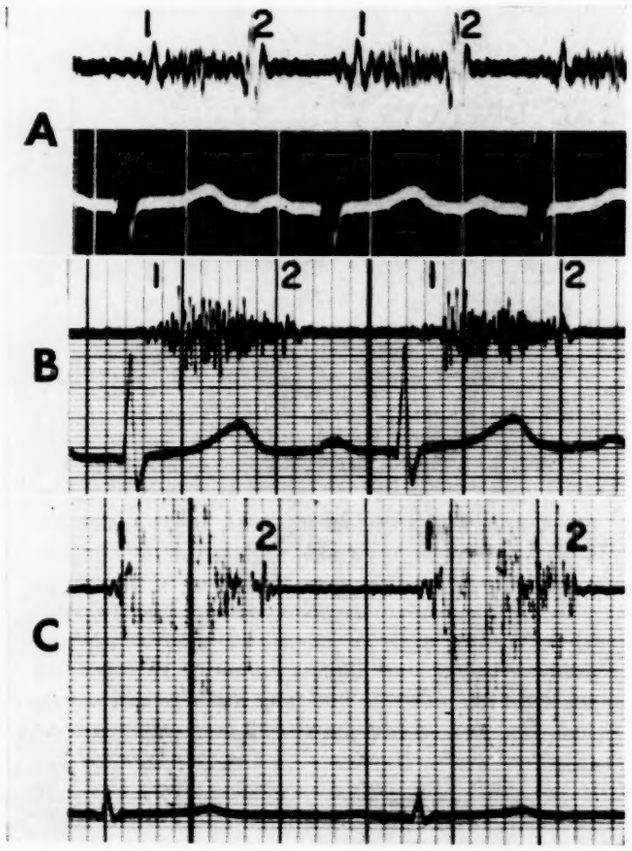


Fig. 1.—*A*, phonocardiogram in case 1 made in April, 1952, over second left interspace, showing loud, normally split second sound. Phonocardiograms, taken over same area in July, 1953 (*B*), and January, 1956 (*C*), showing pulmonary component of second sound to be definitely diminished in intensity.

Report of Cases

Case 1.—A 10-month-old male infant was referred from the Research and Educational Hospitals of the University of Illinois in March, 1952. The patient had had dyspnea, repeated respiratory infections, and a precordial bulge since six months of age. He had never been cyanotic.

Physical examination showed the patient to be a fairly well-developed infant. The patient was dyspneic but not cyanotic. A marked bulge of the anterior wall of the chest was present. The heart was enlarged, and the apex beat was felt in the fifth left intercostal space at the anterior axillary line. A systolic thrill was palpated over the second, third, fourth, and fifth intercostal spaces to the left of the sternum. A rough, grade 5 systolic murmur over the same area was most prominent in the third and fourth left intercostal spaces. The second sound was loudest over the pulmonary area (fig. 1). The femoral pulses were normal.

Hematological studies showed a hemoglobin level of 63 (Sahli), red blood cell count of 3,510,000 per cubic millimeter, and a white blood cell count of 8,400 per cubic millimeter. The differential count was normal. Roentgenographic examination

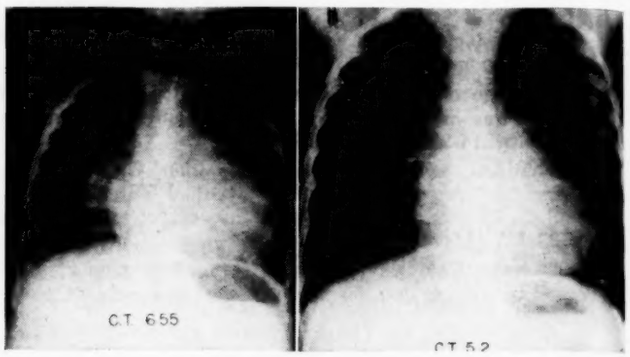


Fig. 2.—*A*, posteroanterior view of chest in patient in case 1 taken in April, 1952, showing transverse diameter of heart to be markedly increased, cardiothoracic ratio to be 0.65, convexity of pulmonary area, and increased pulmonary vascular markings. *B*, same view in patient taken in February, 1956, showing definite diminution of transverse diameter of the heart, cardiothoracic ratio of 0.54, and diminished pulmonary vascular markings, especially in midthird of lung field.

revealed a marked increase in the transverse diameter of the heart, with a cardiothoracic ratio of 0.65 (fig. 2*A*), a convexity of the pulmonary artery segment, and increased pulmonary vascular markings. The right anterior oblique view showed bulging of the pulmonary artery segment. The left anterior oblique view was suggestive of enlargement of both right and left ventricles.

The 15-lead electrocardiogram showed normal sinus rhythm, a rate of 140 beats per minute, an electrical axis of +90 degrees, P-R interval of 0.14 second, wide and notched P waves in lead 1 and aVR, and biphasic P waves in the right precordial leads, with wide and deep downward deflections. There

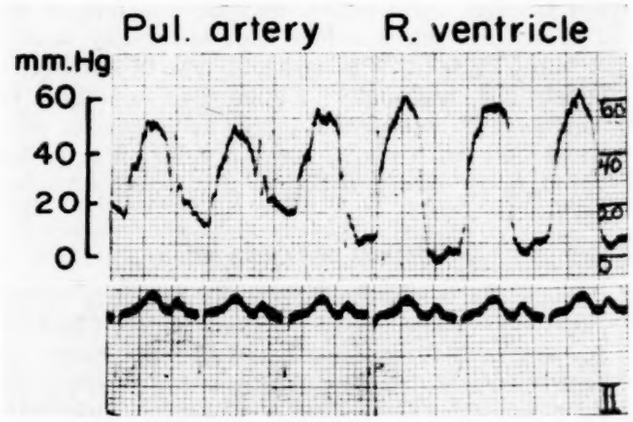


Fig. 3.—Pressure pulse tracing from cardiac catheterization, taken when patient in case 1 was 11 months of age, showing well-defined pulmonary arterial curve that has been attached to right ventricular curve obtained upon withdrawal. Break in continuity of this tracing was made necessary by a run of ventricular tachycardia when outflow was initially entered.

was a QR complex in lead aVF, the R wave measuring 22 mm., and the sum of R_2 and R_3 was 47 mm. The tracings in precordial leads V_2, V_3, V_4, V_5, and V_6 were biphasic and of high voltage. The electrocardiogram was interpreted as indicative of left atrial and right and left ventricular hypertrophy.

The dextroangiocardiogram in the posteroanterior view demonstrated definite blanching of the outflow tract of the right ventricle and increased pulmonary blood flow. On the levoangiocardiogram, there was reopacification of the pulmonary artery, without reopacification of the right atrium.

Catheterization of the right side of the heart performed in April, 1952, revealed hypertension in the right ventricle and pulmonary artery (fig. 3). Analysis of the blood samples for oxygen content demonstrated a large left-to-right shunt at the ventricular level. The pulmonary blood flow was four times that of the systemic flow (see table).

The patient was seen in the clinic again in February and November, 1954. Physical examination showed the patient to be a very active, well-developed child. The patient had a systolic thrill that was felt best over the second and third intercostal spaces and a harsh, grade 4 systolic murmur that was loudest over the third and fourth left intercostal spaces. Roentgenographic examination at this time showed a relative decrease in the size of the heart and a definite decrease of the pulmonary vascular markings as compared with the films from 1952, even though the pulmonary vascular markings still appeared increased above normal. The configuration of the heart indicated left atrial and, probably, right and left ventricular enlargement. The electrocardiogram did not significantly differ from that taken in 1952.

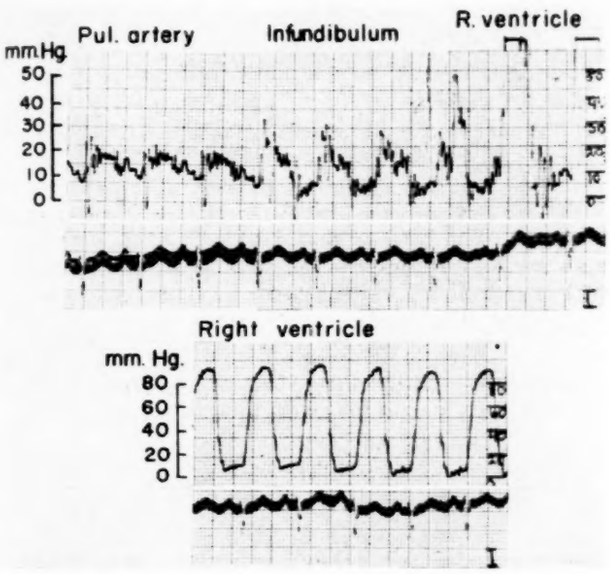


Fig. 4.—Series of matched segments of continuous pressure tracing from cardiac catheterization taken in patient in case 1 at constant sensitivity of pressure system as catheter was successively drawn back from pulmonary artery to infundibular chamber and into markedly hypertensive right ventricular inflow tract. Inflow portion of right ventricular tracing goes off scale at this sensitivity, and, therefore, this portion of pulse pressure curve is repeated below at less sensitive range of manometer.

In February, 1956, the patient was readmitted for further studies. At this time he was asymptomatic, but there was questionable cyanosis. There was a definite bulge over the precordium. The point of maximum impulse was in the fourth left intercostal space in the midclavicular line. There was a systolic thrill felt in the second and also in the first and third left interspaces. A harsh, grade 4 systolic murmur was heard over the same area. The second sound was markedly diminished over the second left intercostal space. Roentgenographic examination showed a decrease in the transverse diameter of the heart and a cardiothoracic ratio of 0.54 (fig. 2). The pulmonary vascular markings appeared normal or slightly decreased as compared with those seen on previous examinations. There was no evidence of left atrial enlargement in the right anterior oblique view. The left ventricle in the left anterior oblique view was definitely enlarged. The dextroangiocardiogram revealed a questionable blanching of the outflow tract of the right ventricle.

The 15-lead electrocardiogram showed a rate of 95 beats per minute, sinus rhythm, a P-R interval of 0.16 second, right axis deviation of +105 degrees, tall R waves measuring 25 mm. in lead V_1, time of the onset of the intrinsicoid deflection longer over the right precordial leads (0.04) than over the left (0.03), and no evidences of left atrial enlargement. The R wave in aVF measured 14 mm., and the sum of R_3 and R_4 was 34 mm.

Catheterization of the right side of the heart was performed in March, 1956; there was now a low level of pressure in the pulmonary artery, 15/6 mm. Hg, and in the infundibulum. In the lower portion of the outflow tract of the right ventricle, marked hypertension resembling the systolic pressure in the

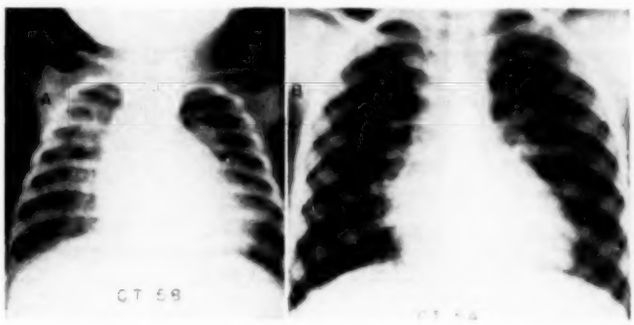


Fig. 5.—*A*, posteroanterior view of chest taken in patient in case 1 in May, 1953, showing cardiothoracic ratio of 0.58, marked increase in pulmonary vascular markings, and aorta arched to right. *B*, same view taken in January, 1957, showing cardiothoracic ratio of 0.52 and pulmonary vascular markings still increased.

femoral artery was recorded (fig. 4). Analysis of the blood samples for oxygen revealed an increase in the oxygen content in the right ventricle over that in samples from the atrium and vena cava. The peripheral arterial oxygen saturation was less than normal, suggesting some mixing by right-to-left shunt, although the major shunt was left to right and amounted to twice the systemic flow. In summing up, cardiac catheterization demonstrated the presence of an infravalvular stenosis, marked right ventricular hypertension, and bidirectional mixing, predominantly from left to right (see table).

Case 2.—A female infant, born Oct. 28, 1952, was first admitted to this hospital on May 6, 1953, for a diagnostic examination. A heart murmur was noted in the patient at 6 weeks

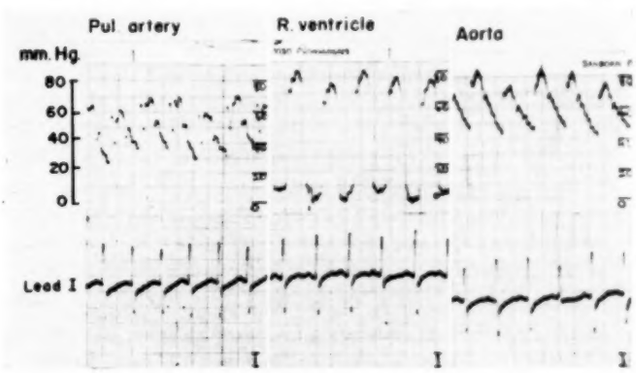


Fig. 6.—Selected strips of tracing of cardiac catheterization taken in patient in case 2 at 9 months of age, showing a well-formed pressure pulse tracing of pulmonary artery slightly lower in its systolic range than right ventricular systolic pressure obtained upon withdrawal. The aortic tracing has a systolic pressure similar to that of right ventricle. Pressure differential between pulmonary artery and right ventricle in presence of large left-to-right shunt is considered normal.

of age, and, at that time, the child was treated for pneumonia at a local hospital. She had repeated respiratory infections, and, three weeks prior to the first admission, the patient was hospitalized in another hospital for treatment of failure of the left side of the heart. Physical examination at the time of the first

admission showed the patient to be a somewhat pale infant who was dyspneic. There was no clinical evidence of cyanosis. Blood pressure level was 110/80 mm. Hg in the right arm and 118 mm. Hg systolic in the left leg. On percussion the heart was noted to be markedly enlarged to the left. A loud, grade 4 systolic murmur was heard over the whole precordium and posteriorly to the right of the midline in the interscapular area.

Roentgenographic and fluoroscopic examinations showed marked enlargement of the transverse diameter of the heart, with a cardiothoracic ratio of 0.58 (fig. 5*A*). The pulmonary artery was straight. The left anterior oblique view suggested the presence of left ventricular enlargement, and there was evidence of enlargement of the left atrium in the right anterior oblique view. A barium esophagram showed that the aorta arched to the right. The pulmonary vascular markings and pulsations were increased.

The electrocardiogram revealed a heart rate of 120 beats per minute, an axis deviation of +75 degrees, notching of the P waves in lead 1 and aVR, and tall P waves in lead 2. Over the right precordial leads the P waves were biphasic and of greater amplitude than normal. The R waves of the QRS complexes in aVR and in the right precordial leads were of high voltage. The T waves were upright over the right precordium. These changes were interpreted as evidence of left atrial and right ventricular hypertrophy. The dextroangiocardiogram in the posteroanterior view presented questionable blanching of the right ventricular outflow tract, and there was continuous opacification of the pulmonary artery in the levoangiocardiogram.

Cardiac catheterization, performed in June, 1953, revealed hypertension in the right ventricle and in the pulmonary artery (fig. 6) and evidence of left-to-right shunt at the ventricular level. The left ventricle and aorta were entered via the ventricular septal defect (see table).

Results of Cardiac Catheteri

Case No.	Sex	Age	B.S.A.,* Sq. M.	Blood Oxygen Contents, Vol. %						
				Inferior Vena Cava	Superior Vena Cava	Right Auricle	Right Ventricle	Pulmonary Artery	Left Ventricle	Aorta
1	M	11 mo.	0.36	8.97	8.25	8.32	11.3	12.3	13.3	
		4 yr., 9 mo.	0.62		9.80	9.64	12.1	13.1		14.9‡
2	F	9 mo.	0.37		8.72	8.02	10.5	10.7	12.0	12.6
		4 yr.	0.68	10.9	10.2	10.3	12.1	13.3	14.0	14.3

* B.S.A. = body surface area.
† Numbers in parentheses are mean blood pressure levels.
‡ Pressure and sample from femoral artery.

While in the hospital, the patient had several long episodes of respiratory difficulty with inspiratory retractions and wheezing. The patient was given 0.02 mg. of digitoxin daily until June, 1954. At that time she appeared clinically to be well. Since then, she has been seen about twice a year in the outpatient clinic, and she has been doing quite well, has not been unusually tired after exercise, and has not been subject to repeated respiratory infections.

In January, 1957, the patient was admitted to the hospital for reevaluation. Physical examination showed the patient to be a well-developed, fairly well-nourished girl who had slight dyspnea but no cyanosis. The heart rate was 108 beats per minute, and the respiratory rate was 28. There was moderate bulging of the left side of the chest. The point of maximum impulse was felt in the sixth left intercostal space, 1 cm. outside the midclavicular line. There was a systolic thrill over the third, fourth and fifth left intercostal spaces that was felt best over the fourth interspace. The first heart sound was loud and of maximal intensity at the apex. The second sound was split and loudest over the third left intercostal space. The third heart sound was constantly heard at the apex. A grade 5, harsh systolic murmur was heard over the whole precordium, but it was loudest over the fourth and fifth left intercostal spaces. A grade 2 diastolic rumble was audible at the apex.

Roentgenographic examination of the chest showed the transverse diameter of the heart to be within normal limits, and the cardiothoracic ratio was 0.52 (fig. 5*B*). The pulmonary artery segment was slightly convex. The pulmonary vascular markings were normal or only slightly increased as compared with those seen on previous examination. There was, again, evidence that the aorta arched to the right but no evidence of left atrial enlargement.

The electrocardiogram showed a heart rate of 105 beats per minute, sinus rhythm, electrical axis of +105 degrees, notching of the P waves in lead 1, biphasic P waves in the right precordial leads, and incomplete right bundle-branch block.

Catheterization of the right side of the heart was performed in January, 1957. The pulmonary artery pressure level was now only slightly elevated, being less than one-half of the systolic level observed in the patient during infancy (fig. 7). Upon withdrawal the catheter entered an infundibular chamber in which the systolic pressure exceeded that in the artery. Further withdrawal caused the catheter to enter an area of marked hypertension in the right ventricle in which the systolic pressure simulated that of the systemic systolic pressure. This patient still had a normal peripheral arterial oxygen saturation, and the estimated pulmonary flow exceeded the systemic flow.

Comment

Findings in Cases.—The patient in case 1 at the age of 10 months showed all the typical clinical and laboratory findings indicative of a large ventricular septal defect. The presence of dyspnea, the bulge over the anterior wall of the chest, the marked cardiac enlargement, the systolic thrill, the rough, grade 5 systolic murmur, maximum over the third and fourth left interspaces, the loud second sound over the pulmonary area, the roentgenologic findings of increased pulmonary vascular markings and pulsations, and the electrocardiographic evidences of left atrial

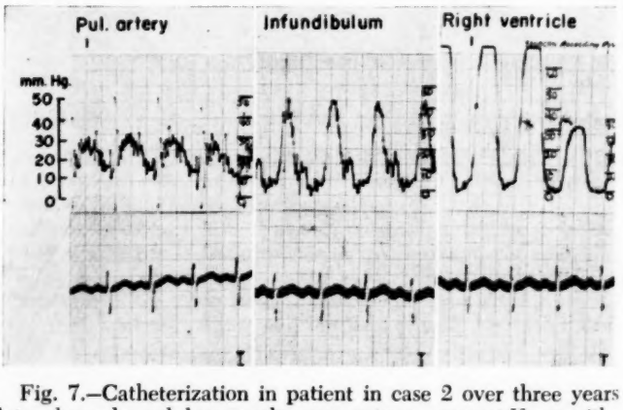


Fig. 7.—Catheterization in patient in case 2 over three years later showed much lower pulmonary artery pressure. Upon withdrawal into outflow tract of right ventricle, ventricular-type pressure curve of fairly symmetrical proportion with diastolic level near 5 mm. Hg and systolic peak exceeding that of artery was noted. Further withdrawal from this infundibular chamber was attended by abrupt rise in pressure at junction of outflow and inflow tracts. This portion of ventricular tracing is shown at two sensitivities of the pressure system to depict true amplitude of pressure curve in millimeters of mercury.

and ventricular hypertrophy are characteristic of this malformation. The diagnosis was further strengthened by the dextroangiocardiogram, which showed blanching of the outflow tract of the right ventricle, by the later reopacification of the pulmonary artery in the levoangiocardiogram without reopacification of the right atrium, and, finally, by the even more conclusive findings on catheterization of the right side of the heart. The original findings on catheterization were those of definite hypertension in the right ventricle

zation in Two Patients

Saturation, %	Hemoglobin, Gm./100 Cc.	Right Auricle	Pressures, Mm. Hg†							
			Right Ventricle	Infundibulum	Pulmonary Artery	Pulmonary Wedge Pressure	Left Auricle	Left Ventricle	Aorta	Pulmonary/Systemic Flow Ratios
95.6	10.6	(7)	66/6 (31)		56/18 (41)	(11)	(8)	69/3 (34)		4:1
91.2	12.1	(6)	89/2 (39)	17/0 (8)	15/6 (11)				83/49 (61)‡	2:1
94.1	9.9	(5)	83/0 (36)		70/25 (53)			85/4 (43)	88/50 (68)	
94	11.2	(2)	77/3 (19)	46/5 (21)	32/12 (19)	(9)			80/53 (66)	

and pulmonary artery, a marked increase in the oxygen content of blood samples from the right ventricle as compared with those from the right atrium, and a normal peripheral arterial oxygen saturation. Pulmonary blood flow was calculated to be more than four times that of the systemic flow. Reexamination in February, 1956, when the patient was over 4 years of age, showed the second sound over the pulmonary area to be definitely diminished instead of being loud and booming as on previous examinations. This was confirmed by phonocardiographic studies (fig. 1*C*). The cardiothoracic ratio as seen on the roentgenograms was also decreased, and the pulmonary vascular markings and increased pulsations were not as prominent as observed on previous roentgenologic examinations. The electrocardiogram at this time revealed more marked evidence of right ventricular hypertrophy and no evidence of left atrial hypertrophy. Of even greater importance, cardiac recatheterization, performed about four years after the first catheterization, revealed definite evidence of localized infundibular stenosis, with lower pressure in the pulmonary artery and marked right ventricular hypertension of even greater extent than on the first catheterization. The left-to-right shunt at the ventricular level was less, and the saturation level in peripheral arterial blood was now somewhat lower than normal. The pulmonary blood flow was about twice that of the systemic flow, rather than four times as on the previous catheterization.

In case 2 all the clinical and laboratory findings of a large ventricular septal defect were also present. The physical, fluoroscopic, roentgenographic, electrocardiographic, angiocardiographic, and cardiac-catheterization findings were typical of this malformation. Here again, later follow-up studies revealed findings typical of ventricular septal defect and localized infundibular stenosis. Both of these patients, like many of our other patients with large ventricular septal defects, presented a marked improvement in their general health and well-being, as compared to the marked dyspnea and repeated respiratory infections they had had during the first years of their lives.

Possible Explanations of Transformation.—What are the possible explanations for this natural transformation of ventricular septal defects into what is apparently another entity? In the experience of one of us and Fell,[1] isolated ventricular septal defects are the most common type of congenital malformations of the heart. During the past 10 years we studied 336 patients with this malformation. The natural course of patients with this malformation is not definitely known. We accept the generally held opinion that some patients with ventricular septal defect develop findings indicative of the Eisenmenger complex, usually in the second or third decade of life.[2] It is interesting to note that Eisenmenger first reported his original case as one of ventricular septal defect, and, in another article[3] about one year later, he emphasized his views regarding the dextroposition of the aorta. Selzer brought out the fact that the morphologic distinction between ventricular septal defects and the Eisenmenger complex presented more difficulty at autopsy than had been appreciated until recently. This view had been previously expressed and accepted in the German literature. It is now generally accepted that, in the presence of a large ventricular septal defect involving the membranous and upper part of the muscular ventricular septum, the aorta appears to come in contact with both ventricles.

Cournand and co-workers,[4] Abrahams and Wood,[5] Broadbent and co-workers,[6] Moffitt and co-workers,[7] Rudolph and co-workers,[8] Magidson and co-workers,[9] and Sell and co-workers[10] have reported a number of patients with pulmonary stenosis and ventricular septal defects, with left-to-right shunts at the ventricular level and normal peripheral arterial oxygen saturation, as separate entities. This combined entity was known previouly in the Spanish literature, and Dr. Augustin Castellanos y Gonzalez named it the "bilogy."[11]

Recently Rowe, Vlad, and Keith[12] reported four noncyanotic infants showing the clinical features of a large ventricular septal defect in whom further studies suggested the diagnosis of tetralogy of Fallot of an atypical type. Their examination of the patients showed evidence of definite pulmonic stenosis, large left-to-right shunt at the ventricular level, right ventricular hypertension equaling the systemic systolic level, and normal arterial oxygen saturation both at rest and with exercise. They based their diagnosis of atypical tetralogy of Fallot on the above findings, the catheter entry into the aorta from the right ventricle, the contour of the right ventricular pressure pulse in two cases, and the occurrence in one patient of an aorta arched to the right. In one patient the diagnosis was confirmed at autopsy.

The presence of an aorta arching to the right in patients with ventricular septal defects should no longer be considered strongly indicative or even suggestive of the presence of a tetralogy of Fallot. Becu and co-workers [13] recently reported an incidence of aorta arching to the right of 6% in 50 patients with ventricular septal defects the presence of which was proved by autopsy. It is now generally recognized that the presence of what appears to be a definite overriding of the aorta in patients with ventricular septal defects does not necessarily mean that some of the venous blood from the right ventricle is shunted into the aorta.[14] This shunting of venous blood from the right ventricle into the aorta will only take place in patients with isolated ventricular septal defects and high pressure in the pulmonary artery or in patients with ventricular septal defects and infundibular stenosis, when the resistance at the pulmonary arterial level in the first group of patients or the infundibular level in the second group exceeds that in the systemic circuit.

At the present time, there appears to be no unanimity in the literature as to the clinical differentiation of patients with ventricular septal defect with organic infundibular stenosis from the group of patients with the atypical tetralogy of Fallot. We believe that it is best to designate patients as belonging to the group of patients having atypical types of tetralogy of Fallot without clinical cyanosis only if their peripheral arterial oxygen saturation is below normal. Actually, one type may merge into the other if the resistance of the outflow tract of the right ventricle increases.

We have records of 15 patients [15] who have had clinical, angiocardiographic, and cardiac-catheterization studies and who showed definite evidences of large ventricular septal defects, with pulmonary stenosis and left-to-right shunts. The systolic pressure gradient between right ventricular pressure and pressure in the pulmonary artery of up to from 60 to 70 mm. Hg certainly excludes a "relative" pulmonary stenosis. Four of these patients have aortas arching to the right, and several of them have evidences of a small right-to-left shunt of insufficient degree to cause clinical cyanosis, in addition to a large left-to-right shunt at the ventricular level; these patients who show diminished peripheral arterial oxygen saturation but who are still clinically noncyanotic belong to the group with the so-called atypical tetralogy of Fallot, while the others belong to the group with ventricular septal defects, with infundibular stenosis and only left-to-right shunts. Several of these 15 patients, who have been followed up for a number of years, have shown at some stage of observation typical auscultatory, radiologic, and electrocardiographic evidence of isolated large ventricular septal defects. However, none of these patients had cardiac-catheterization studies at this early stage, and, therefore, we cannot prove that such a transformation took place.

Do the above cases mentioned in the literature and our own 15 cases show entities different from large ventricular septal defects? Or is it possible that some of these patients, very early in life, had evidences of only a large ventricular septal defect, later on developed hypertrophy of the crista supraventricularis and, perhaps, of its septal or parietal band, and, still later, in their natural courses presented unmistakable findings of associated infundibular stenosis of a high degree? Our two cases reported here certainly prove this to be true. The frequency with which large ventricular septal defects undergo such a transformation in their natural course is at present not known. We do not mean to imply that the majority of patients with organic infundibular stenosis and ventricular septal defects or acyanotic types of tetralogy of Fallot have simple ventricular septal defects in the newborn period. On the other hand, we cannot definitely exclude this possibility. We are, of course, continuing our studies, and we hope that this discussion will lead to a reevaluation of the present-day concepts of the pathogenesis of ventricular septal defects, infundibular stenosis with ventricular septal defects, and atypical noncyanotic types of tetralogy of Fallot. It is possible that the unity of origin of these three entities will in the future be firmly established. The development of infundibular stenosis in patients with large ventricular septal defects and the decrease in the left-to-right shunt appear to be a natural protective mechanism limiting the large pulmonary blood flow and possibly explaining the improvement in the general well-being of some patients with large ventricular septal defects after the age of one year. This improvement has been noted and commented upon by many authors.[16]

Edwards [17] and his associates, Dammann,[18] and others have shown the important role of the pulmonary vascular bed in adjusting the systemic and pulmonary blood flows in response to a common systemic and pulmonary ejectile force and a large pulmonary blood flow. They have shown that the presence of these two factors initiates the gradual and progressive elevation of the pulmonary vascular resistance and that this increased resistance is due to the persistence of the fetal state of the pulmonary arterioles with their thick media and, in addition, to the new formation of intimal changes that may even lead to thrombosis of these arterioles. We believe that the clinical and hemodynamic data in our two cases prove that changes in the cardiac musculature of the outflow tract of the right ventricle further play an important role in the adjustments between the pulmonary and systemic circulations.

The autopsy records of the Cook County Hospital, the Research and Educational Hospitals of the University of Illinois College of Medicine, and the Presbyterian Hospital show that 27 cases of ventricular septal defects occurred in children. The ages at death of the 27 were as follows: stillborn four, one day in three from one to seven days in two, from one to four weeks in five, from one to three months in five, from three to six months in five, and 14 months in one. No autopsies have been performed in the pediatric age group in patients with ventricular septal defects who were over 14 months of age. These records appear to point to two possibilities: Either the overwhelming majority of patients with ventricular septal defects do not die during childhood once they pass the age of 14 months, or in some of them, the percentage being unknown so far, the defects are transformed in their natural course into ventricular septal defects with infundib-

ular stenosis or into tetralogy of Fallot. This concept leads to some very pertinent questions involving the pathology and the clinical, roentgenologic, electrocardiographic, angiocardiographic, and cardiac-catheterization findings in patients with ventricular septal defects. The concept also brings up important considerations in the medical and surgical management of these patients, particularly because of the present availability of open heart surgery for these patients.

Summary

Two patients who in infancy presented typical clinical and physiological data indicating the presence of large ventricular septal defects developed, approximately four years later, characteristic clinical and hemodynamic data indicating ventricular septal defects with localized infundibular stenosis or clinically noncyanotic type of tetralogy of Fallot.

We have demonstrated a new concept of the unity of large ventricular septal defects with ventricular septal defects and infundibular stenosis or tetralogy of Fallot in some cases. The frequency of this natural transformation is at present not known. This concept introduces important considerations in the diagnosis and medical or surgical management of patients with ventricular septal defects.

Addendum

Since this paper was submitted for publication, an additional seven patients have been restudied, with examination including cardiac recatheterization. All of these patients had their first cardiac catheterization during their first year of life and a recent recatheterization from three to five years later.

Four of these patients still present all the clinical and physiological evidences of a large ventricular septal defect. One of them now shows clinical and physiological findings typical of tetralogy of Fallot. At the age of 2 months this patient had a pressure level in the right ventricle of 85/3 (44) mm. Hg and in the pulmonary artery of 87/5 (44) mm. Hg, and the peripheral arterial oxygen saturation was 95.8 vol. %. On recatheterization when the patient was 38 months of age, the pressure level in the right ventricle was 87/5 (42) mm. Hg, in the pulmonary artery the mean pressure was 13 mm. Hg, and the peripheral arterial oxygen saturation was 74.3 vol. % at rest.

The other two patients, who during infancy had shown moderate right ventricular and pulmonary hypertension, now present normal pressure levels in the right ventricle and in the pulmonary artery but still have a left-to-right shunt at the ventricular level.

700 S. Wood St. (12) (Dr. Gasul).

This study was supported, in part, by a grant from the Chicago Heart Association.

References

1. Gasul, B. M., and Fell, E. H.: Salient Points in Clinical Diagnosis of Congenital Heart Disease, J. A. M. A. **161**:39-44 (May 5) 1956.

2. Selzer, A., and Laqueur, G. L.: Eisenmenger Complex and Its Relation to Uncomplicated Defect of Ventricular Septum: Review of 35 Autopsied Cases of Eisenmenger's Complex, Including Two New Cases, A. M. A. Arch. Int. Med. **87**:218-241 (Feb.) 1951.

3. Eisenmenger, V.: Ursprung der Aorta aus beiden Ventrikeln beim Defect des Septum Ventriculorum, Wien. klin. Wchnschr. **11**:25, 1898.

4. Cournand, A.; Baldwin, J. S.; and Himmelstein, A.: Cardiac Catheterization in Congenital Heart Disease: Clinical and Physiological Study in Infants and Children, New York, Commonwealth Fund, 1949.

5. Abrahams, D. G., and Wood, P. H.: Pulmonary Stenosis with Normal Aortic Root, Brit. Heart J. **13**:519-548 (Oct.) 1951.

6. Broadbent, J. C.; Wood, E. H.; and Burchell, H. B.: Symposium on Cardiac Catheterization: Left to Right Intercardiac Shunts in Presence of Pulmonary Stenosis, Proc. Staff Meet. Mayo Clin. **28**:101-106 (Feb. 25) 1953.

7. Moffitt, G. R., Jr., and others: Pulmonary Stenosis with Left to Right Intracardiac Shunts, Am. J. Med. **16**:521-527 (April) 1954.

8. Rudolph, A. M.; Nadas, A. S.; and Goodale, W. T.: Intracardiac Left-to-Right Shunt with Pulmonic Stenosis, Am. Heart J. **48**:808-816 (Dec.) 1954.

9. Magidson, O., and others: Pulmonary Stenosis with Left to Right Shunt, Am. J. Med. **17**:311-321 (Sept.) 1954.

10. Sell, G. G. R., and others: Physiological Studies in Cases of "Tetralogy of Fallot" with Little or No Overriding of Aorta, read before the second World Congress of Cardiology, Washington, D. C., Sept. 16, 1954.

11. Castellanos y Gonzalez, A.: Cardiopatias congénitas de la infancia, Havana, M. V. Fresneda, 1948.

12. Rowe, R. D.; Vlad, P.; and Keith, J. D.: Atypical Tetralogy of Fallot: Noncyanotic Form with Increased Lung Vascularity: Report of Four Cases, Circulation **12**:230-238 (Aug.) 1955.

13. Becu, L. M., and others: Anatomic and Pathologic Studies in Ventricular Septal Defect, Circulation **14**:349-364 (Sept.) 1956.

14. McCord, M. C., and Blount, S. G., Jr.: Complications Following Infundibular Resection in Fallot's Tetralogy, Circulation **11**:754-760 (May) 1955.

15. Gasul, B. M.: Dillon, R. F.; Vrla, V.; and Hait, G.: Unpublished data.

16. Kjellberg, S. R.; Mannheimer, E.; Rudhe, U.; and Jonsson, B.: Diagnosis of Congenital Heart Disease: Clinical and Technical Study by Cardiologic Team of Pediatric Clinic, Karolinska Sjukhuset, Stockholm, Chicago, Year Book Publishers, Inc., 1955.

17. Edwards, J. E.: Structural Changes of Pulmonary Vascular Bed and Their Functional Significance in Congenital Heart Disease, 26th Ludvig Hektoen Lecture, Proc. Inst. Med. Chicago, **18**:134-146 (June 15) 1950.

18. Dammann, J. F., Jr., and Muller, W. H., Jr.: Role of Pulmonary Vascular Bed in Congenital Heart Disease, Pediatrics **12**:307-325 (Sept., pt. 1) 1953.

Black Skin Lesion.—Six cases of a lesion simulating a melanoma clinically but due to an aneurysmal dilatation of a capillary with thrombosis are presented. The necessity of distinguishing these tumors from malignant melanomas is stressed. The thesis that every black, flat, growing lesion is not a melanoma is emphasized. Therefore, it follows that wanton sacrifice of adjacent normal tissue is not indicated in such lesions unless there is histologic proof or indisputable clinical evidence of malignancy. This is not to be construed as advocating that one should minimize the growing flat black nodule nor that histologic examination is not essential in such cases. —E. Epstein, M.D., F. G. Novy Jr., M.D., R. A. Skahen, M.D., and M. E. Krause, M.D., Melanoma-Simulating Nodules Due to Capillary Aneurysms, *California Medicine*, July, 1956.

PRESENT-DAY DIAGNOSIS AND TREATMENT OF PHEOCHROMOCYTOMA

A REVIEW OF FIFTY-ONE CASES

Walter F. Kvale, M.D., Grace M. Roth, Ph.D., William M. Manger, M.D.
and
James T. Priestley, M.D., Rochester, Minn.

• *The histories of 50 patients who were found to have pheochromocytomas have been analyzed in order to identify factors that might be important in diagnosis and prognosis. The hypertension characteristic of pheochromocytoma was paroxysmal in 26 and persistent in 24. The tumors are usually benign, but eight in this series were malignant, and seven of the malignant type occurred in the cases of persistent hypertension. Tests for pheochromocytoma should be carried out on patients who complain of spells of severe headache of unexplained cause with perspiration, thoracic and abdominal pain, and nervousness and on any hypertensive patient who is thin and young, who has hypermetabolism without other signs of hyperthyroidism, who give a paradoxical reaction to ganglion-blocking agents, and who responds to anesthetics with a blood pressure rise. The tests consist of the administration of histamine base, tetraethylammonium chloride, phentolamine, or piperoxan and determinations of plasma pressoramines under certain standard conditions. For removal of the tumor a transverse upper abdominal incision is recommended because it gives access to both adrenals and permits the inspection of the abdomen for aberrant masses of adrenal tissue which are especially likely to occur in the region of the great vessels in the abdomen and about the base of the mesentery of the small intestine. During operation constant attention to the blood pressure is necessary because the pressure often rises sharply when the tumor is handled and falls to dangerously low levels when the tumor is removed. When recurrences or metastases are encountered, it is still possible to prolong the life of the patient by surgery or roentgenotherapy.*

The diagnosis of functioning pheochromocytoma is becoming less difficult as experience increases. Careful appraisal of the history and close scrutiny of the patient's age, weight, and body build and certain laboratory data will often afford a clue at the first or second interview.

Since the first pharmacological test [1] for pheochromocytoma was introduced, we have had the opportunity at the Mayo Clinic of studying carefully 51 patients who had pheochromocytomas. It is the purpose of this paper to present pertinent data on the diagnostic aspects and results in 50 of these cases, to demonstrate that the diagnosis can be made if the possibility of this condition is kept in mind, to summarize indications for performing pharmacological and other tests for pheochromocytoma, and to show that the transabdominal approach [2] should be used and that cure is usually but not always possible. Pheochromocytomas usually arise from the adrenal medulla.

Classification

The grouping of patients with hypertension caused by pheochromocytoma into those who have paroxysmal hypertension and those who have sustained hypertension has been largely an arbitrary one. In general those patients whose tumors were secreting epinephrine and arterenol (nor-epinephrine) intermittently had paroxysmal hypertension. Those patients whose tumors were secreting pressor substances continuously had persistent hypertension. However, the latter group may have attacks also during which the blood pressure is even higher than usual.

Twenty-six of our 51 patients were classed as having paroxysmal hypertension. All of the 26 complained of spells associated with a marked increase in the blood pressure. Between their spells, the blood pressure was normal. Twenty-four patients were placed in the group of those who had persistent hypertension. Although their blood pressure was elevated persistently, in some it would be normal or approach normal at times. The periods of elevated blood pressure sometimes were associated with spells, although not all patients had them. One patient was considered to have pheochromocytoma which was symptomatically nonfunctioning and was found on exploration of a retroperitoneal mass. He had no symptoms of a pheochromocytoma and no hypertension before operation. This case will not be considered in further discussion except for minor points.

From the Section of Medicine (Dr. Kvale), the Section of Physiology (Dr. Roth), and the Section of Surgery (Dr. Priestley), Mayo Clinic and Mayo Foundation. Dr. Manger is a Fellow in Medicine, Mayo Clinic and Mayo Foundation. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Read before the 10th Clinical Meeting of the American Medical Association, Seattle, Nov. 27, 1956.

Symptoms

Paroxysmal Hypertension.—All of the patients with paroxysmal hypertension complained of spells or attacks. Headache of varying intensity, but usually extremely severe, was the commonest symptom and was present in all except one case. Sweating and palpitation were the next commonest symptoms. Also present were tachycardia, great anxiety, nervousness, pallor or flushing of the face, nausea and vomiting, pain in the chest and abdomen, pain and numbness in the legs, and tingling and coldness of the hands and feet. In any one case, one or more of these symptoms could be lacking.

The duration of the illness varied from 6 weeks to 10 years, the usual time being 2 to 5 years. The length of the history had no bearing on the secondary vascular damage which the intermittent discharge of the pressor amines might produce. One woman who had been having excruciating bouts of headaches as frequently as several times a week for 10 years had normal ocular fundi and a normal vascular system. On the other hand a man, aged 38 years, who had had symptoms for only eight months suffered both a coronary occlusion and thrombosis of the basilar artery before the diagnosis could be made.

The frequency of the attacks also varied from as often as 10 to 25 a day, to once a day or even to only once every 2 to 3 months. They usually lasted only 10 to 15 minutes, but some persisted only a few seconds and others for several hours or days. Weakness and exhaustion commonly followed an attack. The usual story was that the attacks increased in frequency but not in severity. This was often an important point in differentiating the attacks from migraine. Between attacks the patients were generally in good health.

Persistent Hypertension.—The 24 patients classed as having persistent hypertension had more or less continuous hypertension. However, 10 complained of attacks similar to those experienced by patients with only paroxysmal hypertension. During these attacks the blood pressure rose to even higher levels. The usual picture was that of increasingly severe headaches, excessive perspiration, nervousness, palpitation, tremulousness, and loss of weight. All 24 patients with persistent hypertension were thin. If the condition has been unrecognized, conditions due to secondary vascular damage, such as loss of vision, coronary occlusion, cerebrovascular thrombosis, and congestive heart failure, may be the chief complaints.

Symptoms had been present for 3 weeks to 16 years, with the average being 3 to 4 years. The duration of the symptoms closely paralleled the duration of the hypertension, although in one case hypertension was not discovered for five years after the onset of symptoms.

Findings at Examination

Paroxysmal Hypertension.—The average age of patients with paroxysmal hypertension was 44 years, ranging from 26 to 59. They tended to be older than those in the group with persistent hypertension. Only one patient was in the 20's; most (10) were in their 30's.

Height ranged from 5 ft. 2 in. to 6 ft. (157 to 183 cm.). The average height of 21 patients was 5 ft. 5 in. (165 cm.). The patients also tended to be thin, ranging in weight from 106 to 192 lb. (48 to 87 kg.), with the average weight of 134 lb. (61 kg.). The patient who weighed 192 lb. was 5 ft. 10 in. (178 cm.) tall.

The fasting level of blood sugar was determined in 25 of the 26 patients during normotensive levels. Values above normal were found in 11. The basal metabolic rate was determined in 25 of the 26 patients. Values were more than +20% in four, the highest being +33%. They were between +11 and +20% in 5 and normal in 15. The basal metabolic rate was of aid in making the diagnosis of pheochromocytoma in only six cases. In general the basal metabolic rate and level of blood sugar were not of material help in making the diagnosis in this group.

Aortograms, perirenal injections of air, and presacral injections of oxygen have not been used by us because localization actually is not considered necessary before operation. These procedures also entail an unnecessary risk. Excretory urograms were made in all cases. They gave evidence of a mass above one of the kidneys or displacement of the kidney in 7 of the 26 cases. Of interest is the following case.

CASE 1.—The patient brought her retroperitoneal pneumograms with her; they showed a mass at the lower pole of the left kidney. The excretory urograms also showed what appeared to be a mass in the lower pole of the left kidney. On exploration, however, the pheochromocytoma was found on the right side. A cyst was found in the lower pole of the left kidney and left undisturbed.

In other words, the excretory urograms were of help in locating only six of the seven tumors.

Persistent Hypertension.—The average age of 24 patients with known functioning pheochromocytomas was 35.6 years, ranging from 12 to 67 years. However, 16 of the 24 were less than 40 years of age and only 2 were more than 60, being 67 and 65 years respectively.

The average height of 20 of the 24 patients was 5 ft. 5 in. The average weight of 23 of the 24 patients was 121.8 lb. (54.9 kg.). Only five of these patients weighed more than 134 lb. The two heaviest, weighing 169 and 160 lb. (77 and 73 kg.), were both 5 ft. 10 in. tall. Eleven weighed 113 lb. (51 kg.) or less. The range in weight was 90 to 169 lb. (41 to 77 kg.). These patients generally were much thinner than those with paroxysmal hypertension. The one patient with a nonfunctioning pheochromocytoma was 6 ft. tall and weighed 227 lb. (103 kg.).

The basal metabolic rate was determined in 21 of the 24 patients. It ranged from +8 to +101% and was more than +20% in 16. Hypermetabolism without hyperthyroidism was of significant help in making the diagnosis in 18 of these cases. In only three of the cases was the basal metabolic rate less than +10%.

Hypermetabolism was the clue in making the diagnosis in the following case.

CASE 2.—A man, aged 34 years, registered at the clinic in September, 1954. He had had headaches, sweating, shortness of breath, and hypertension for 16 years. Examination revealed evidence of old healed rheumatic heart disease. Pheochromocytoma was suspected, but two histamine tests were negative because the patient was taking antihypertensive drugs. The last dose was taken on the morning of the test. The first phentolamine (Regitine) methanesulfonate test was equivocal and the second was more positive. The basal metabolic rate on two occasions was +39 and +42%. Determination of the pressor amines revealed greatly elevated values. A pheochromocytoma was removed from the right adrenal gland.

The blood sugar level was determined in 17 of the 24 patients. It ranged from 107 to 256 mg. per 100 ml., and in 10 patients was 120 mg. or more.

The excretory urogram was of help in localizing the tumor in 4 of 24 cases and also in the case of a nonfunctioning pheochromocytoma. In one case, however, the urogram indicated that the tumor might be on the right, whereas actually it was found to be on the left.

Tests

Drugs.—Four drugs have been used almost exclusively in testing this group of patients for pheochromocytoma. Histamine base [1] and tetraethylammonium chloride [3] have been used when patients were suspected of having a pheochromocytoma causing paroxysmal hypertension. Histamine has been used oftener because it has given a more precise result. A dose of 0.05 mg. of histamine base in 0.5 ml. of isotonic solution of sodium chloride is injected rapidly intravenously. The result is considered positive when, after a drop in 30 seconds, blood pressure rises significantly, with a maximum at the end of two minutes, above the level reached in the cold pressor test. The importance of the cold pressor test in interpreting the results of the histamine test cannot be overemphasized. It is as much a part of the histamine test as the injection of histamine.

Phentolamine [4] and piperoxan have been used for the patient suspected of having a pheochromocytoma that is causing sustained hypertension. Results of the phentolamine and piperoxan tests are considered positive if the blood pressure decreases more than 35 mm. Hg systolic and 25 diastolic from the basal level and remains decreased for three or four minutes. A slight decrease in the blood pressure in the first two minutes after intravenous injection of the drug with a return to basal level is not a positive result. Five milligrams of phentolamine is injected rapidly for the phenotolamine test, and 10 to 20 mg. of piperoxan is injected slowly for the piperoxan test. Phentolamine has not caused any serious side-reactions in our experience and, therefore, we have used it more frequently. Piperoxan will cause a pressor response in individuals who have essential hypertension.

Before a pharmacological test is made on a patient suspected of having a pheochromocytoma, the basal blood pressure should be determined. Drugs, such as narcotics, sedatives, and cyanates, should be withheld for at least 48 hours before tests, as they may produce false-positive results. Antihypertensive drugs will produce false-negative results and (hydralazine [Apresoline] hydrochloride at least) should be withheld for 14 to 16 days before these tests.

Since any patient with pheochromocytoma may have wide fluctuations of blood pressure, the drug to be employed for testing depends entirely on the basal blood pressure. When the blood pressure is less than 170 mm. Hg systolic and 110 diastolic, histamine is the drug of choice, but, if the basal blood pressure is more than 170/110, phentolamine is the drug of choice. When the blood pressure rose greatly after the injection of histamine, phentolamine was employed to lower the blood pressure. Both histamine and phentolamine may thus be used for the same patient having a pheochromocytoma, and positive results from the two tests for the tumor may be obtained.

Pharmacological tests have been of great aid in making a diagnosis of pheochromocytoma, but they are not always successful or accurate. Results were positive for pheochromocytoma in all cases of paroxysmal hypertension except one, inconclusive in three cases of persistent hypertension, and positive in all other cases of persistent hypertension.

If the results of the histamine or phentolamine tests are doubtful or negative, then the test should be repeated or a test with one of the other drugs employed. No single test is always completely reliable. If doubt still exists, measurement of the quantity of pressor amines in the blood at the level of the highest blood pressure is indicated.

Pressor Amines.—Chemical quantitation of pressor amines in the blood is the most direct and accurate clinical method of establishing the presence of a functioning pheochromocytoma. However, a pheochromocytoma must either be secreting epinephrine or arterenol spontaneously or the sample of blood for analysis should be collected at the height of the blood pressure response to histamine. Otherwise the findings of a normal concentration of pressor amines in a sample do not exclude pheochromocytoma.

With a modification [5] of the method of Weil-Malherbe and Bone, the pressor amines have been measured in the plasma of 15 of our patients with pheochromocytoma and persistent hypertension and of 10 with pheochromocytoma and paroxysmal hypertension. The findings in 13 of these patients have been reported previously.[5A] In all but one of the patients with persistent hypertension, the concentration of pressor amines was elevated significantly, that is, to more than 3.5 mcg., of epinephrine-like substance per liter of plasma. This one patient, however, had a normal concentration of pressor amines when the blood pressure was 182/110 mm. Hg. When histamine base was administered intravenously, the blood pressure increased to 264/164 mm. Hg and the concentration of pressor substances rose to 15.8 mcg. per liter of plasma.

Of the 10 patients with paroxysmal hypertension tested, 2 had normal concentrations of pressor amines when the blood pressure was normal. However, when the blood pressure was highest during the histamine tests, pressor amines were significantly elevated above normal in all 10 patients.

The concentration of pressor amines is nearly always less than 3.5 mcg. per liter of plasma in cases of essential hypertension. The concentration is not significantly increased after stimulation with histamine in patients without pheochromocytoma. There is evidence that the concentration of pressor amines in plasma may be lowered by some of the antihypertensive drugs.[6] However, to our knowledge, these drugs have not decreased the plasma concentration to the normal range in patients with pheochromocytoma. We have found increased concentrations of pressor amines in some patients with renal insufficiency, jaundice, increased intracranial pressure, and lymphoma. (It is uncertain whether the substance measured as pressor amines in patients with renal insufficiency or lymphoma is primarily epinephrine or arterenol.) Thus, it is important to realize that other conditions may cause elevated concentrations of pressor amines which may lead to a false diagnosis of pheochromocytoma if the results of this test are relied on solely. Hemolysis or hyperbilirubinemia or both can interfere with the chemical analysis and cause erroneously elevated concentrations of pressor

substances. Only under conditions in which the tumor is actively secreting the pressor amines will the results of the tests for pressor amines be positive. Finally, it is important to remember that elevated concentrations of pressor amines may result from the use of some epinephrine-like substances. We have observed this in one patient with asthma who was using nebulized epinephrine. Even the use of some vasoconstrictor agents for nasal stuffiness is under suspicion at the present time as a cause of elevated plasma pressor amines.

Findings at Operation

Paroxysmal Hypertension.—In the present series of cases the first operation for pheochromocytoma causing paroxysmal hypertension was performed in 1943 and the last in 1956. There were no extra-adrenal tumors in this group of 26 cases.

At the time of operation 19 tumors were removed from the right adrenal gland and 5 from the left adrenal gland. In two additional cases the tumors were bilateral. In one case of bilateral tumors, two tumors were removed from the right adrenal and one from the left. In the other case of bilateral tumors, the one on the right was removed but the one from the left was not.

Case 3.—This patient was operated on for gallstones. At exploration, bilateral adrenal tumors were found also. The pheochromocytoma on the right was removed but the one on the left was not disturbed. A histamine test performed after operation gave a positive result. The tumor on the left side was still present seven years after operation when the patient replied to an inquiry. The patient, however, was well, although she had mild hypertension.

This is the only case in which a pheochromocytoma was not suspected before operation.

Seven of the 26 patients had gallstones. These were found either before, at the time of, or after removal of the pheochromocytoma. The large percentage of gallstones in this series of cases suggests more than a coincidence.

Persistent Hypertension.—The first operation for pheochromocytoma causing persistent hypertension in this series of patients was performed in 1946 and the last in 1956. There were 13 tumors in the right adrenal gland, 13 in the left adrenal gland, and a total of 6 extra-adrenal tumors; 3 of the extra-adrenal tumors were inoperable metastatic masses at the time of operation. One was retroperitoneal on the left side, and one was situated behind the structures at the hilus of the liver. In one patient who had multiple tumors, three arose from the right adrenal, one arose from the left adrenal, and an additional tumor was found behind the right lobe of the liver. In one case previously reported,[7] two more tumors were found along the aortic chain at reoperation. This made a total of 32 tumors in the 24 patients. The patient previously mentioned who had had no hypertension also had an extra-adrenal tumor. None of the 24 patients had gallstones.

Type of Tumor and Results

Paroxysmal Hypertension.—In the 26 cases of paroxysmal hypertension all tumors except one were benign.

Case 4.—A benign pheochromocytoma was removed from the right adrenal gland of this woman in July, 1952. Severe headaches recurred three years later. At reexploration in July, 1955, a firm fixed mass in the region of the right adrenal gland and metastasis to the liver were found. Roentgenologic treatments were given, and as of this date, she is living but is not well.

Follow-up information was obtained on 24 patients. All except two are living. One of the two who died had active pulmonary tuberculosis at the time of operation and subsequently died of this disease, and the other died from causes other than his pheochromocytoma 10 years after his tumor was removed. Five patients have had further difficulty: one had residual effects from a cerebral infarction; one had had metastasis found at reoperation and treated roentgenologically; the other three had only minor difficulty. Seventeen are living and well.

Persistent Hypertension.—In four of the cases of persistent hypertension in which the tumors were histologically benign the lesions recurred subsequently or metastasized. In three of the four cases, the tumor when removed was thought to be benign but metastasis occurred; in one of these three cases (case 5) a cure was thought to have been obtained before the metastasis developed.

Case 5.—A man, aged 36 years, had had headaches and sweating for only five weeks before operation for pheochromocytoma in 1954. Both adrenal glands were normal, but a benign tumor was found and removed from behind the hilus of the liver. Convalescence was uneventful; blood pressure during the first two postoperative days did not exceed 140/90 mm. Hg and averaged 110/80. It then increased slowly to 150/100. Headaches and sweating had disappeared, and pharmacological tests for pheochromocytoma gave negative results. Six months later an enlarged lymph node was removed from the left supraclavicular region. It proved to contain a pheochromocytoma—histologically the same as the tumor removed at abdominal operation. Symptoms returned. Radical dissection of the neck and axilla on the left with excision of a segment of the clavicle was done in March, 1955. Metastatic pheochromocytoma involved six axillary nodes and four lower and midjugular nodes. Roentgenologic treatment and phenoxybenzamine (Dibenzyline) hydrochloride gave some relief, but he died on Feb. 20, 1956. Autopsy revealed extensive metastasis in the ribs and vertebrae, lungs, liver, and along the inferior vena cava.

Case 6.—On Jan. 30, 1956, a histologically benign pheochromocytoma was removed from the right adrenal gland of a woman, aged 67 years. After operation, blood pressure remained elevated, the pain in the arm persisted, and the concentration of pressor amines was greatly elevated. There was no obvious clue as to site of the metastasis or another pheochromocytoma. She died four months later. Autopsy disclosed extensive metastasis to the liver, lung, and retroperitoneal and mediastinal regions.

Case 7.—The original tumor was benign, but metastasis occurred in the rib. Other pheochromocytomas have been removed from this boy. He is still living six years after his first operation but has metastasis to the second and third thoracic vertebrae and the seventh rib which have been treated by roentgen rays. This case has been reported in detail elsewhere.[7a]

Case 8.—An adenocarcinoma, grade 2, of the tail of the pancreas was removed at the same time that an apparently benign pheochromocytoma was removed from the right adrenal gland. This patient, a woman aged 36 years, lived for eight years and subsequently died of metastasis thought to be secondary to the carcinoma of the pancreas. Autopsy revealed

the metastasis, presumably from carcinoma of the pancreas, and also a recurrent pheochromocytoma on the right side. This gives evidence that these tumors can recur.

In one other case, a malignant pheochromocytoma was found at operation. This patient died two months later of metastasis. In three cases, inoperable fixed pheochromocytomas were found at operation and the patients died soon afterward of metastasis.

Results: Seven of the 24 patients with persistent hypertension had potentially fatal pheochromocytoma, and 6 of these have died from maligant pheochromocytoma. The seventh has had recurrent tumors removed and is still living, although he has metastasis. Another died, presumably from metastasis from a carcinoma of the pancreas, and still another after sympathectomy.

The other 15 are living and well, although one has residual homonymous hemianopsia that developed during the postoperative period. Three have residual mild hypertension. In all cases in which the changes in the retinal vessels were those of hypertension, group 3 or 4, the changes have reverted to those of hypertension, group 1 or 2.

Surgical Aspects

Frequent determination of blood pressure and its proper control constitute one of the most important procedures during operation on a patient who has pheochromocytoma. It is advisable to have a medical assistant in addition to the anesthesiologist present at the operation. The sole responsibility of the medical assistant is the determination and recording of blood pressure at intervals of one or two minutes, during the entire operation. In some cases such close observation may not be necessary, but in others it may prove to be virtually lifesaving.

Characteristically the blood pressure fluctuates widely during removal of a pheochromocytoma. It usually rises sharply with induction of anesthesia. This rise commonly continues as the incision is made and becomes more pronounced as the tumor is palpated and mobilized. Subsequently, after the tumor is removed, the blood pressure falls precipitously to shock levels. This drop is usually most marked in patients who have experienced persistent hypertension preoperatively. Actually, if this drop does not occur at this time, the presence of an additional tumor which has not been removed should be suspected. Because of these wide fluctuations in blood pressure, which may have serious results if not properly treated, it is essential to have depressor as well as pressor agents readily available during operation.

It is our practice always to insert a needle in a vein and start a slow infusion of 5% solution of dextrose before induction of anesthesia. Phentolamine in amounts of 5 mg. is used as the depressor agent, and levarterenol (Levophed) in amounts of 4 mg. is used as the pressor agent. When blood pressure rises with induction of anesthesia, it may be advisable to inject phentolamine. This is always true as the tumor is palpated and mobilized. Subsequently, after removal of the tumor, levarterenol is employed. If blood pressure does not fall after removal of a tumor, further confirmation of another tumor may be obtained by administration of phentolamine, which, under these circumstances, may be expected to cause a definite decrease in blood pressure. The exact type of anesthesia may not be a matter of great importance, but it has been our practice to induce anesthesia with thiopental sodium followed by nitrous oxide and oxygen and supplemented with a small amount of curare as needed.

Various surgical approaches, such as the posterolumbar and even the transthoracic, have been used in operations for pheochromocytoma. It is our belief that a transverse upper abdominal incision is the approach of choice. This type of exposure permits simultaneous exploration of both adrenal glands through a single incision and also affords opportunity for general abdominal exploration. It makes examinations for localization of a tumor in one adrenal gland, such as perirenal or presacral injection of air or aortography, unnecessary, since both adrenal glands are routinely palpated and inspected at operation. Exploration of the abdomen and opposite adrenal gland from a posterolumbar incision on one side has never been too satisfactory in our experience.

Although it is true that usually pheochromocytoma is a single, benign tumor which occurs in one adrenal gland, these tumors may be multiple on one side, bilateral, malignant, and located wherever chromaffin tissue is found. Because of the possibility of multiple, bilateral, or ectopically located tumors, both adrenal glands should be explored in every patient and in addition general abdominal exploration should be performed. Particular attention is given to the region of the great vessels in the abdomen and the base of the mesentery of the small intestine. A pheochromocytoma may be located in the thorax or even elsewhere in the body, and, if the clinical diagnosis appears to be definite and exploration of the adrenal glands and abdomen fails to reveal a tumor, search in other regions must be considered. Fortunately, almost every patient who has a pheochromocytoma is thin, which facilitates the abdominal approach. This, of course, is in contrast to patients who have adrenal cortical hyperfunction (Cushing's syndrome), who are usually obese.

Appropriate postoperative care after removal of a pheochromocytoma is extremely important. This is likely to be particularly true if the patient has had sustained hypertension preoperatively. The main concern during the postoperative period is maintenance of an adequate level of blood pressure. The pronounced hypotension which becomes evident on removal of a functioning pheochromocytoma may persist for hours or several days after operation unless proper supportive measures are employed. These patients should be kept under constant observation, with frequent determinations of blood pressure until reasonable levels of blood pressure persist without support. It is our practice during the period of pronounced hypotension to use a slow but continuous drip of a liter of 5% solution of dextrose to which 4 mg. of levarterenol has been added.

One need not, and preferably does not, endeavor to maintain blood pressure at a high level which might correspond with the preoperative level. Maintenance of systolic pressure just above the renal secretory level or in the vicinity of 100 to 110 mm. Hg gives entirely satisfactory results. The amount of levarterenol which is given is gradually reduced as normal physiological responses permit. A word of caution against prolonged use of a single vein or too high concentration of levarterenol should be expressed, as under these circumstances local irritation leading to necrosis of tissue may occur.

Indications for Tests for Pheochromocytoma

One of the problems in diagnosis is when should a pheochromocytoma be suspected and laboratory tests for pheochromocytoma ordered? Our data indicate that patients of the following types should be scrutinized with the possibility of pheochromocytoma in mind, and, if other possibilities are ruled out, it might be wise to perform pharmacological tests on them:

1. Any patient who complains of spells associated with headache, perspiration, thoracic and abdominal pain, nervousness, and vasomotor phenomena should have a pharmacological test. In 25 of our patients with paroxysmal hypertension, the histamine test was positive for pheochromocytoma. In one case the negative test was the result of antihypertensive drug. The diagnosis was made after estimation of the concentration of pressor amines in blood drawn when the blood pressure was high during an attack. In another patient the histamine test gave a positive result when it was performed after cholecystectomy, at which time bilateral pheochromocytomas were found. The one on the right was removed. The diagnosis had been suspected before operation in all except one case (case 3), either by the home physician on the basis of the elevated blood pressure during a spell or by the home physician and by us on the basis of the history and of positive results of tests for pheochromocytoma.

2. Thin patients with a history of fluctuating hypertension which is within normal limits on examination should have a histamine test. All other thin people with hypertension should undergo the appropriate test. The average weight of 23 of the 24 patients with functioning pheochromocytomas and persistent hypertension was 121.8 lb. Three weighed 160 lb. or more. Two of these were 5 ft. 10 in. tall, but the rest averaged 5 ft. 7.5 in. (171 cm.) or less. Eleven weighed 113 lb. or less. This seems to exclude the obviously obese patient with hypertension, for to our knowledge pheochromocytomas are not likely to occur in this group. Recently we have seen a somewhat obese patient (not included in this report) in whom our preoperative diagnosis of pheochromocytoma was confirmed at operation.

3. All young individuals with hypertension should be tested. Only 3 of our 24 patients with persistently functioning pheochromocytomas were more than 50 years old. Sixteen were less than 40. If the phentolamine tests in these individuals are negative or equivocal, they should be repeated, other tests performed, or concentration of pressor amines determined.

4. All individuals with hypermetabolism without hyperthyroidism should be investigated. In 16 patients with persistently functioning pheochromocytomas, the basal metabolic rate was more than +20% and hyperthyroidism and other causes of hypermetabolism had been excluded. In one case (case 2) in which the phentolamine test was equivocal because of previous antihypertensive drugs, the basal metabolic rate was +39 and +42% on two occasions. After stimulation with histamine, blood for determination of concentration of pressor amines was drawn and found to be markedly positive.

5. All individuals with a short history of hypertension should be considered for tests. In one of our patients, a girl 18 years old, hypertension had been known for only three weeks, and in two patients hypertension was discovered on examination at the clinic. The symptoms of hypertension, however, ordinarily closely approximate the known duration of the hypertension.

6. All individuals with severe hypertension, group 2, 3 or 4, who have not been previously included in these categories should undergo tests. Fifteen of the 24 patients with persistently functioning pheochromocytomas had ocular evidence of hypertension of group 3 or 4.

7. Patients who respond in a paradoxical reaction to the ganglionic blocking agents should be considered for pharmacological tests. In one of our patients, marked elevation of the blood pressure occurred after the initial hypotensive reaction from subcutaneously injected hexamethonium.

8. When a patient responds unsatisfactorily to an anesthetic and the blood pressure rises, the administration of anesthetic should be stopped immediately, for this could indicate a pheochromocytoma. This was true in our first case of persistent hypertension. Pharmacological tests should be performed on such a patient.

Comment

It is not to be presumed that the diagnosis of pheochromocytoma is not difficult. Pheochromocytoma producing paroxysmal hypertension produces few problems. In all of the 26 cases, with one exception (case 3) in which the tumor was found at the time of cholecystectomy, the diagnosis was suspected clinically by the referring physician or by a physician at the clinic. The histamine test was positive in all cases except one. In the latter case, estimation of the pressor amines at the level of the highest blood pressure reading, after histamine stimulation, made the diagnosis.

Pheochromocytoma producing persistent hypertension presents more problems. The diagnosis was suspected clinically in 18 of the 24 cases. Significant is the fact that it was not suspected clinically in the first three cases and the pharmacological tests were not conclusive in two of these cases but were positive in the third. As experience increased, the condition was thought of more seriously. In one case the diagnosis was not actually suspected clinically, but the fact that the patient had malignant hypertension and

was only 18 years old led to pharmacological tests, which were positive. In case 2, pheochromocytoma was considered but the diagnosis was not actually made until plasma pressor amines had been quantitated after hypermetabolism had been discovered and after the pharmacological tests were inconclusive. In one case false-negative results were first obtained from the pharmacological tests, the reason being that the patient had been taking hydralazine. After use of this drug was discontinued, tests gave positive results, and a pheochromocytoma was found at operation.

Important clues to the diagnosis of pheochromocytoma in patients with persistent hypertension are increasingly severe headaches, sweating, palpitation, nervousness, tremulousness, loss of weight, thinness, relatively young age, and hypermetabolism. All or some of these may be missing.

In the seven years from 1943 through 1949, 580 patients were sent from the diagnostic services to the vascular laboratory to be tested for the presence of pheochromocytoma (tables 1 and 2). In this same period approximately 37,000 patients were given a diagnosis of hypertension at the clinic. This figure includes those patients who return from year to year. Thus, only 1.6% of all hypertensive patients were tested for pheochromocytoma.

During the succeeding years, the number of patients tested included those tested for both paroxysmal and sustained hypertension, utilizing histamine and phentolamine chiefly, and, on many occasions, both on the same patient. No serious side-reactions have occurred. When the blood pressure became alarmingly

TABLE 1.—*Findings in Tests for Pheochromocytoma Given at Mayo Clinic, 1943-1955*

Yr.	Tests Made, No.	Persons Tested, No.	Patients with Hypertension, Total No.	% Tested*	Pheochromocytoma: Paroxysmal	Pheochromocytoma: Persistent
1943-1949		580	37,000	1.6	7	4
1950	479	378	6,300	6.0	1	3
1951	1,140	696	6,200	11.2	5	3
1952	1,093	684	6,200	11.0	2	1
1953	1,393	864	6,200	13.9	3	2
1954	2,183	1,076	6,200	17.4	5	8
1955	1,495	769	6,200	12.4	1	2
Total		5,047†	74,300	67.9	24	23

* Not all patients tested had hypertension.

† These figures in tables 1 and 2 are not the same because the total of 5,047 patients tested may have had one or more of the various tests for pheochromocytoma. Thus, 4,158 patients had one or more phentolamine (Regitine) tests with or without histamine or other tests; 3,755 had one or more histamine tests with or without phentolamine and other tests; and 1,274 had one or more other type of test for pheochromocytoma with or without histamine and phentolamine tests. Table 1 also carries data for 9 months less than table 2.

high after stimulation with histamine, it could be lowered immediately by administration of phentolamine.

Each year at the clinic approximately 6,200 patients are given a diagnosis of hypertension. In 1950, 378 patients underwent pharmacological tests for pheochromocytoma. This was approximately 6% of all patients with hypertension who were tested in the laboratory for pheochromocytoma. This percentage gradually increased to 17.4 in 1954, then fell to 12.4 in 1955.

During the years 1943 through 1949, about 2,400 tests of all kinds were performed on 580 patients. Eleven cases of pheochromocytoma were found during this time. During the years 1950 to 1955, 7,783 tests were performed on 4,467 patients. During this period 36 cases were found. Three have been found in 1956 up to the time of writing.

Ideally, all patients with hypertension should be tested for pheochromocytoma. There are reasons which make this impossible, or perhaps impractical. Obesity

TABLE 2.—*Types of Tests for Pheochromocytoma Given at Mayo Clinic, 1943-1956*

Type of Test	Tests, No.	Patients, No.	Date
Phentolamine (Regitine)	4,700	4,158	1950-Oct., 1956
Histamine	4,159	3,755	1943-Oct., 1956
Subtotal	8,859	7,913	1943-Oct., 1956
Other	1,324	1,274	To Oct., 1956
Total	10,183	9,187*	

* See table 1, 2nd footnote.

is hardly ever associated with pheochromocytoma; many patients with hypertension are receiving drugs which may produce false-negative as well as false-positive results on phentolamine tests. The determination of the concentration of pressor amines cannot as yet be used as a routine procedure on all patients with hypertension. However, the vascular laboratory at the Mayo Clinic has performed an unusually large number of tests during the past six and a half years as compared to previous years. We do not know whether the total number of cases of pheochromocytoma diagnosed (39) represents all the cases of pheochromocytoma screened at the clinic. There is, of course, the possibility and probability that cases of pheochromocytoma have been missed but, by following the indications as already noted, we believe that the chance of diagnostic error is minimized.

Summary and Conclusions

From a review of 50 cases of pheochromocytoma diagnosed at the Mayo Clinic from 1943 to October, 1956, the following points emerge.

Pheochromocytomas, although rare, can be detected in many cases by careful appraisal of the history, close scrutiny of the patients' age and weight, and use of either the histamine or phentolamine (Regitine) test or both, which require no more than the usual precautions for any test. If there is any question, determination of the pressor amines in the blood at the level of the highest blood pressure is needed. The tumors seem to be peculiar to thin people, especially those who have persistent hypertension. Those patients with hypertension who are young, are thin, have lost weight, and have hypermetabolism without hyperthyroidism should have the test.

The tumors are usually benign, and removal may prevent secondary vascular changes, such as visual impairment, coronary occlusion, congestive failure, and cerebrovascular accidents, and can be lifesaving. The tumors can be malignant, and some which were first considered benign became malignant and metastasized. They can recur. Therefore, the diagnosis and removal of pheochromocytoma do not always carry a promising outcome. Pheochromocytomas in 16%

(8) of the 50 cases were malignant or have become malignant; the largest number of malignant lesions occurred in cases of persistent hypertension. There seems to be more than a coincidental relationship between gallstones and pheochromocytoma.

Pheochromocytomas can be located anywhere in the abdominal cavity. It is not necessary to localize them preoperatively, since the anterior abdominal approach allows free exploration. After removal of a pheochromocytoma, patients should be examined frequently to be sure that no recurrence has developed or metastasis occurred. If either has occurred, further operative or roentgenologic treatment may prolong the life of the patient.

200 First St. S. W. (Dr. Kvale).

References

1. Roth, G. M., and Kvale, W. F.: Tentative Test for Pheochromocytoma, Am. J. M. Sc. **210:**653-660 (Nov.) 1945.

2. Sprague, R. G.; Kvale, W. F.; and Priestley, J. T.: Management of Certain Hyperfunctioning Lesions of Adrenal Cortex and Medulla, J. A. M. A. **151:**629-638 (Feb. 21) 1953.

3. LaDue, J. S.; Murison, P. J.; and Pack, G. T.: Use of Tetraethylammonium Bromide as Diagnostic Test for Pheochromocytoma, abstracted, Am. J. Med. **3:**118 (July) 1947.

4. Grimson, K. S.; Longino, F. H.; Kernodle, C. E.; and O'Rear, H. B.: Treatment of Patient with Pheochromocytoma: Use of Adrenolytic Drug Before and During Operation, J. A. M. A. **140:**1273-1274 (Aug. 20) 1949. Gifford, R. W., Jr.; Roth, G. M.; and Kvale, W. F.: Evaluation of New Adrenolytic Drug (Regitine) as Test for Pheochromocytoma, J. A. M. A. **149:**1628-1634 (Aug. 30) 1952. Goldenberg, M.; Snyder, C. H.; and Aranow, H., Jr.: New Test for Hypertension due to Circulating Epinephrine, ibid. **135:**971-976 (Dec. 13) 1947.

5. Manger, and others: Method for Quantitative Estimation of Epinephrine and Norepinephrine: Preliminary Report, Proc. Staff Meet. Mayo Clin. **28:**526-531 (Sept. 23) 1953.

5A. Manger, W. M., and others: Chemical Quantitation of Epinephrine and Norepinephrine in 13 Patients with Pheochromocytoma, Circulation **10:**641-652 (Nov.) 1954.

6. Burger, M.: Abnahme der Plasma-Noradrenalin-Konzentration nach Reserpin, Helvt. physiol. et pharmacol. acta **14:** C13-C14, 1956.

7. (*a*) ReMine, W. H.; Estes, J. E., Jr.; Dockerty, M. B.; and Priestley, J. T: Hemiplegia Resulting from Pheochromocytoma: Report of Case, J. A. M. A. **152:**808-811 (June 27) 1953. (*b*) Kvale, W. F.; Priestley, J. T.; and Roth, G. M.: Pheochromocytoma: Clinical Aspects and Surgical Results, A. M. A. Arch. Surg. **68:**769-778 (June) 1954.

TREATMENT OF ONE HUNDRED FORTY-EIGHT BURN CASES IN A COMMUNITY HOSPITAL

Merton L. Griswold Jr., M.D., Plainfield, N. J.

• *The mortality percentage for this unselected consecutive series is 5.4. When this figure is contrasted with a 35.2% mortality reported by one university hospital in 1924, considerable improvement in burn therapy is indicated.*

In the experience of our hospital, a reduction in mortality is a result of improvements in both systemic and local treatment. Systemically, the important thing is the quantity of water and electrolytes given intravenously; lactated Ringer's solution has been preferred. When the total surface burned equaled or exceeded 20%, 6 to 8 liters of solution has been given during the first day, after which the volume has been gradually reduced. Locally, wet dressings have been applied under sheets of Pliofilm. Surfaces have been ready for grafting generally about the 15th day. Antibiotics have been used locally only if the surface showed signs of infection, and have been given systemically only when indicated by known complications such as pneumonia. The postage-stamp method of skin grafting has proved invaluable. The fact that 15 of the 148 burns were caused by bonfires or burning trash suggests an important step toward prevention. Attention to the rehabilitation of the burned patient has also been rewarded by some excellent results.

A survey of the literature over the last century would indicate that progress in the treatment of the extensive burn has been spasmodic. There have been many modes of therapy suggested and then discarded. Only recently have we recognized the role of the internist as well as the surgeon in combating the grave systemic disturbances relating to shock and nutrition in these cases.

Mortality and Incidence

Farmer,[1] at the Hospital for Sick Children in Toronto, Canada, has presented a comprehensive analysis of mortality from burns for the years 1913 to 1955. Any series of burn cases to be truly significant should take into account the extent of the individual burn and the age of the patient. There is no selection as to severity in Farmer's series, but the second factor is fairly constant, because all cases reported involve children. The mortality from 1913 to 1924 was 35.2%; from 1925 to 1928, 16.1%; from 1929 to 1937, 11.8%; and from 1938 to 1941, 2.9%.[1] That from 1942 to 1955 was 2.8%.[2]

About 1925, tannic acid spray therapy was instituted and blood transfusions were introduced on a more general scale; this probably accounts for the first significant drop in mortality from burns, from 35.2% in the 1913-to-1924 period to 16.1% in the 1925-to-1928 period. Also, the importance of electrolyte balance was becoming recognized.

The next major mortality decrease was in the 1938-to-1941 period, which marked the advent of the sulfonamides. The 2.8% mortality in the period 1942 to 1955 would indicate that we are approaching the minimum mortality, and this is being accomplished primarily because of better early shock treatment. Probably no great further advances will be made until

it is possible (1) to demarcate and remove the burn eschar earlier and (2) to utilize in skin grafting other sources of skin than the patient's own.

The patient with an extensive burn often dies, for, after the first week, his vitality decreases to the point that he is vulnerable to even a minor complication. If he is very young or over 60 years of age, if he is obese, or if he is an alcoholic or anemic, he has some additional obstacles to hurdle on a margin that is often uncomfortably close, as illustrated in table 1.

TABLE 1.—*Factors Contributing to Mortality in Eight Cases of Extensive Burn*

Case No.	Age, Yr.	Sex	Extent of Burns, %	Survival Time, Days	Contributing Factors
1	89	M	18	14	Malnutrition, senescence
2	82	M	28	11	Sepsis, senescence
3	67	M	10	3	Alcoholism for 6 yr., cirrhosis of liver
4	11	M	42	3	Laryngotracheal bronchitis, fluid intake inadequate
5	68	F	35	9	Hemiplegia 3 yr. before, uremia
6	24	M	80	12	Gangrene of leg, pulmonary embolism
7	75	F	40	12	Senescence, sepsis
8	24	F	28	20	Obesity, avitaminosis with anemia. Partially covered with grafts on 16th day after burn
Av.	55		35	10.5	

Jackson,[3] at the Birmingham, England, Burn Unit, compiled figures from a closely supervised burn service that admits about 400 patients a year and is not selective as to age or severity of burn. There was a steady rise in the number of patients with severe burns admitted between 1948 and 1951. Jackson reported that in 1948 the incidence of full-thickness burns was 59% and the mortality was 3%. In 1949 the respective figures were 68% and 4%; in 1950, 76% and 5%; in 1951, 88% and 7%; and in 1952, 85% and 6%. In the period 1953 to 1956, the incidence of full-thickness burns in the series of 148 patients reported on in this paper was 52%, with a mortality of 5.4% (table 2).

TABLE 2.—*Number of Patients with Various Percentage of Body Surface Damage by Full-Thickness Burn, 1953 to 1956*

	% Body Surface Burned						
	1-10	11-20	21-30	31-40	41-50	51-60	More than 60
Total	41	19	7	6	1	1	2
Children under 3 yr.	4	1	1	1	...	...	...
Deaths	1	1	2	2	1	...	1

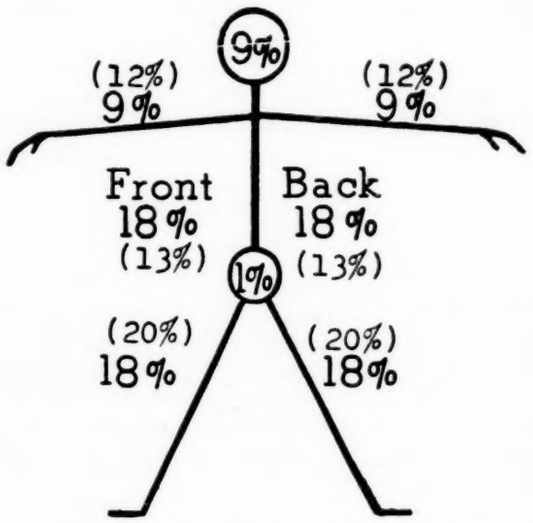
Scrutiny of varied published reports elsewhere would indicate that the over-all mortality runs somewhere between 5 and 15%. Becker and Artz[4] have recently reported on a series of 54 children, all with severe burns. In this group, seven deaths occurred—a mortality rate of 13%.

Program for Burn Treatment

This study is based on a series of 148 patients hospitalized with burns over a four-year period, 1953 to 1956 inclusive. The therapy has been conducted in accordance with a program drawn up in advance and modified subsequently as experience dictated. In the treatment program, we at the hospital, while recognizing that low morbidity and mortality are the aim of any system of therapy, have had to take into consideration the limited bedspace facilities of a community hospital of 437 beds and the ever-present shortage of human power for patient care.

The first problem to confront is the determination of the severity of the burn and whether hospitalization is necessary. If there is doubt as to the depth of the burn and if more than 10% of the total body surface seems to be involved, hospitalization, at least for observation, is wise. If large vesicles are visible or if marked blanching or charring are present, the decision is readily made that deep burns are present. Children do not tolerate initial burn trauma well and may go into primary shock with a not very large burn surface.

One can make a quick evaluation of the surface extent of burns with the "Rules of Nine" of Wallace[5] (see figure). Skerlj and Kulcar[6] have recently published data indicating that according to anthropological tables the trunk should be considered about 25.4% of the total body surface instead of the 36% designated by Wallace. Revision of the upper extremity



"Rules of Nine" by Wallace[5] for measuring burn surface: the head and each arm are 9% of the total body surface and the front of the trunk, back of the trunk, and each leg are 18%. Figures in parentheses represent approximately the revisions suggested by Skerlj and Kulcar.[6]

surfaces from Wallace's 18% to 24.8% is also suggested, with an increase from 36 to 40% in the lower limbs. In summary, the changes of Skerlj and Kulcar would detract from the trunk measurements and add to the extremities.

If the patient is to be transported, placing a clean sheet or towel over the burnt area is advisable to avoid contamination. Blankets may then be placed over the patient for warmth.

Inpatient Treatment

Upon the patient's arrival at the hospital, the concern is for the general condition of the patient, and the treatment of the surface burn is really a secondary matter. If there is any question as to primary shock ensuing, we routinely insert a polyethylene catheter, preferably into the saphenous vein at the ankle.

Intravenous Fluid Therapy.—Lactated Ringer's solution, as advocated by Moyer,[7] is the solution of choice for intravenous administration. Less systemic reaction is manifested, and the risk of hepatitis from pooled plasma is obviated. The use of Hartmann's solution also lessens the risk of acidosis, the occurrence of which is quite possible if sodium chloride solution alone is used. We have used almost no plasma or plasma expanders and entirely agree with the findings of Markley and co-workers [8] as to the value and simplicity of use of the saline solutions. I believe that the quantity of electrolyte is the important thing and, provided the solution is relatively isotonic, its specific make-up is of less significance. Intravenously administered fluid is supplemented by oral doses of buffered salt solution made by dissolving 4 Gm. of salt tablets and 1.8 Gm. of sodium bicarbonate tablets in a quart of iced water to which a few drops of lemon juice have been added for palatability.

What should the total intake be for a patient weighing 70 kg. (155 lb.)? If the total surface burned is 20% or more, we arbitrarily give 6,000 to 8,000 cc. for the first 24 hours and then gradually reduce the amount. A child weighing half as much is allowed only half as much fluid. The urine output in the first 24 hours is usually less than 500 cc. even with this large intake, but the second 24-hour period usually shows a marked increase.

Whole blood has not been used extensively in the primary shock stage, unless there was an anemia present before the burn was sustained. With an actual concentration of all mass in the circulating blood, as manifested by hemoglobin and hematocrit determinations, I believe that whole blood is a source of embarrassment to the circulatory mechanism and may promote sludging. When the hematocrit determination has decreased to 40% or less, which commonly occurs about the 4th to 10th day, the indicated time for transfusion has come, although, if there is a rapid fall in the corpuscular volume earlier than the 4th day, whole blood is given.

As to the plasma expanders, I am inclined to agree with Davis,[9] who has found that both plasma and the expanders disappear rapidly from the circulating blood with very temporary support to the intravascular volume. The lactated electrolytic solutions, to be sure, are also rapidly lost, but their eventual reabsorption and secretion do not present the problems inherent in the use of blood, plasma, or the expanders.

That the employment of saline solutions in the early shock phase is efficacious I believe is substantiated by the fact that, of the eight patients in this series who died, only two did not survive beyond the third day. The factor of human error was involved in one case in that, for some hours, it was not noted that an intravenously placed catheter was functionless. The second death involved an elderly male with relatively minor burns admitted in a state of acute alcoholism with liver enlargement.

Grafting.—We have had trouble in persuading the patient with a small area of deep burn to enter the hospital early for grafting. For example, a 10-cm. burned area will often require two months to heal, while an immediate covering graft reduces the healing time to one week. We believe that the physician caring for a burn wound at home should consider that any areas unhealed after 14 days might well benefit from graft coverage. It should be noted in this series that, whereas the time between hospital admission and the first grafting procedure was 11.02 days (table 3), the time from the date of burn to the first grafting procedure was 22.11 days. Of the patients who underwent skin grafting, 47 underwent only one grafting procedure; 16, 2; 1, 3; 2, 4; and one each, 5, 6, 8, and 11 procedures. Of the eight patients who died, only one survived long enough to undergo grafting.

Healing Time.—Few writers have reported on "mean healing time." Its definition is somewhat empirical, but we have used Jackson's [3] interpretation of the "healing time" as the number of days intervening between injury and complete epithelialization. Jackson computed the mean healing time in his series of patients (1948 to 1951) to be 51 days, while it was 45 days in the series of patients herein reported.

TABLE 3.—*Various Aspects of 148 Consecutive Cases of Burn Treated in the Hospital, 1953-1956*

Mortality		8(5.4%)
Patients with partial-thickness loss of skin, no.		71
Patients with full-thickness loss of skin, (av. age 25.1), no.		77
Males	53	
Females	24	
Children (under 12 yr.)	34	
Adults	43	
Av. surface area burned, %		14.44
Days spent in hospital by patient with skin graft, av. no.		28.73
Days in hospital from admission to first grafting procedure, av. no.		11.02
Days from date of burn to first grafting procedure, av. no.		22.11

Local Treatment

Once it has been determined that there is full-thickness skin involvement, wet dressings are applied. Ordinary towels are soaked in saline solution and applied under sheets of Pliofilm recovered from discarded oxygen tents. The early use of the wet dressing is supported by the work of King and co-workers,[10] as well as Reynolds and co-workers,[11] who reported that immediate cooling of the burned areas by wet compresses effectively decreased local edema, capillary permeability, and mortality in dogs. The towels on the patients can be changed with a minimum of effort daily by the nursing staff, and if Pseudomonas aeruginosa becomes a problem, it can be controlled by using a 1:2,000 solution of chlortetracycline or some similar broad-spectrum antibiotic. We have had no trouble to date with skin allergy.

For patients with circumferential burns of the trunk, the orthopedic revolving bed (Foster or Bradford principle) eliminates the possibility of decubitus ulcer and decreases the hazards of respiratory complications. After considerable experimentation with the chemical and enzymatic agents for removal of the eschar, we have returned to the use of wet dressings. If the cover medium is kept sufficiently moist, some eschar comes away with each removal of the dressing and loose pieces can be removed with forceps and scissors at the bedside.

Preoperative Preparation and Skin Replacement

We have been able, in some instances, to graft as early as the 11th day after the burn, but the average time is about 15 or 16 days. Systemic antibiotic therapy is contraindicated, I believe, because there is no good evidence that its use can combat bacteria at the burn surface. Furthermore, sensitivity may be induced with consequent overgrowth of resistant organisms. Thus the systemic use of antibiotics should be reserved for such known complications as pneumonia, local abscess formation, and cystitis developed after the use of a Foley catheter.

As to the use of adrenal steroids, their use in this series is restricted to the convalescent period and then only for short periods. We have no evidence that epithelial regeneration is aided. Mulholland [12] cites a case treated with corticotropin (ACTH) for 30 days; on the 30th day the patient suddenly died. At autopsy, necrosis of the upper lobe of the right lung caused by aspergilli was found.

Suppuration is less in the early stages of slough separation. It is advantageous, we believe, to alternate open exposure of the granulating surface with applications of moist dressings. This process "rocks" the bacteria and allows neither the aerobic or anaerobic types to gain ascendency. As the healing proceeds, exposure to air is increased, because 80% of the bacterial organism consists of water and without moisture it cannot flourish.

TABLE 4.—*Causes of Burns*

	Patients, No.
Christmas tree	1
Hot radiator	3
Industrial tar or hot metal	8
Cooking grease	3
Bonfire	15
Smoking in bed or chair	10
Cooking scalds	12
Lighting or playing with matches	4
Gasoline, careless use of	6
Dwelling-house fire	1
Costume	1
Hot water bottle	1
Scald, steam pipe	1
Firefighting, professional	1
Stove ignition, while cooking	2
Heating radiator fluid	2
Acid from cauterization (dog bite)	1
Illuminating gas explosion	3
Oil stove	1
Paint remover explosion	1

The technique for removal of skin is a matter for the individual operator. I have preferred the dermatome with adhesive tape backing, which will remove up to 28 sq. in. of skin on one tape.

Homoplasty has been resorted to in four instances only and then from living donors. By reusing the donor areas at eight-day intervals and starting grafting early, skin shortage can usually be overcome. The postage-stamp method is invaluable and positively indispensable on areas such as the chest, where respiratory movement may cause dislodgment of the graft. The loss of a 2-in. piece is of no moment, whereas loss of a large piece approaches a disaster.

The tape-backed skin is not sutured on. It is held in place with elastoplast strips, or else multiple thickness gauze rolls may be draped over the areas, as the granulations soon adhere to the coarse gauze and prevent slipping. The donor areas are dressed with plastic strip dressings; this lessens adherence to the raw area upon removal four to five days later.

As the unhealed areas become smaller, it is feasible to use local anesthetization when skin is removed. As many as three dermatome drums can be removed by this method, and the patient's fluid or food intake by mouth is not disturbed. This is important in his customary state of progressive debilitation.

Rehabilitation and Prevention

One of our patients sustained a 60% total surface burn and survived, and the actual monetary cost of his 117-day stay in the hospital was found to be about $4,800. This does not take into account any fees for the physicians involved but covers only such hospital expenses as bed occupancy, medicaments, and transfusions. The patient's weekly wage of $70 was lost for 18 months; this his family could ill afford. The residual effects on the patient, both physical and psychological, tend to have an adverse effect on his future earning capacities. This patient did return to his previous occupation as a laboratory assistant. It is also heartening to note that of the other patients with severe burns who survived all returned to their former occupations, although some plastic revision of scars, which had been deferred, was necessary.

Table 4 itemizes the causes of some of the more severe burns as derived from the charts of patients.

The predominating cause of burns was bonfires or burning trash. The spectacle of children stamping out burning embers is seen far too often. Scalds occur usually when a vessel of hot water is upset; they can be prevented, in some instances, by keeping the handles of cooking utensils in positions where they could not easily be grasped by a child. Ignition of clothes from smoking in bed or a chair is certainly preventable. The patients with the most extensive burns in this last category were stupefied by intoxicants. One rather unusual cause of burns was the overenthusiastic use of acid as a cauterization treatment for a dog bite.

The average medical practitioner is prone to consider burn patients, except those with minor burns, as candidates for hospital admission. He can play an important role in burn treatment by pointing out to the family that most severe burns occur in the home and that, like most home accidents, they do not need to happen.

It is doubtful if much attention is paid to the flammability of fabrics when they are purchased by the average housewife. I recently discussed the problem with the head of a large textile company, and the fact was brought out that there is very little demand for fire-resistant fabrics and that much more could be done in the way of coating fabrics to reduce the spread of the flame. Some children's costumes have been banned after the children have been burned, thus bringing the matter to the attention of the lawmakers. These accidents have usually happened because there have been open candles at parties. Untreated cotton is one

of our most highly flammable fabrics and is the material used almost universally in such common articles as bed sheets and shirts.

In general, flame will travel rapidly from the point of ignition on any cotton or linen fabric. Wool, nylon, and Orlon will only burn at the point of contact and are, therefore, quite fire resistant. Silk and rayon are less vulnerable to fast burning than are cotton or linen. We are certainly not going to exist without using fire, and the above discussion suggests one avenue that we can pursue to reduce the destruction.

Comment

The planned regimen for the patient with a deep burn has been set up in order to conserve hospital manpower as well as to lower mortality and morbidity rates. In this series of 148 patients with burns who were treated as inpatients during a four-year period in one institution, orally and intravenously given saline solutions, rather than colloids, have been preferred in the early shock phase. The complications have seemed to be less with the saline solutions. As a general rule, the burned area is enclosed in a continuous wet towel dressing, which is comfortable for the patient and simplifies change of the dressing. Dry eschar does not form around the joints, and movement is thus encouraged. The eschar is macerated, thus allowing its daily removal at the bedside with less operative trauma necessary for its separation and removal. The over-all mortality in the series of 148 patients has been 5.4%. For the patients who underwent skin grafting, the average hospital stay amounted to about 29 days.

There are many unsolved problems in the treatment of the patient with an extensive burn, but it does seem possible to say that our best results are obtained in those institutions or units where the personnel are familiar with the problems likely to be incurred during both the acute and rehabilitative phases.

947 Park Ave.

References

1. Farmer, A. W.: Experience with Burns at Hospital for Sick Children, Am. J. Surg. **59**:195-209 (Feb.) 1943.
2. Farmer, A. W.: Personal communication to the author.
3. Jackson, D. M.: Treatment of Burns: Exercise in Emergency Surgery; Hunterian Lecture, Ann. Roy. Coll. Surgeons England **13**:236-257 (Oct.) 1953.
4. Becker, J. M., and Artz, C. P.: Treatment of Burns in Children, A. M. A. Arch. Surg. **73**:207-215 (Aug.) 1956.
5. Wallace, A. B.: Treatment of Burns, Practitioner, **170**:109-118 (Feb.) 1953.
6. Skerlj, B., and Kulcar, Z.: Surface Areas of Body Parts and Their Possible Implications in Treating Burns, Brit. J. Plast. Surg. **9**:165-167 (July) 1956.
7. Moyer, C. A.: Assessment of Therapy of Burns: Clinical Study, Ann. Surg. **137**:628-638 (May) 1953.
8. Markley, K., and others: Clinical Evaluation of Saline Solution Therapy in Burn Shock, J. A. M. A. **161**:1465-1473 (Aug. 11) 1956.
9. Davis, J. H., and others: Effect of Capillary Permeability on Maintenance of Plasma Volume Following Administration of Dextran and Albumin, S. Forum **5**:455-461, 1954.
10. King, T. C.; Reynolds, L. E.; and Price, P. B.: Local Edema and Capillary Permeability Associated with Burn Wounds, S. Forum **6**:80-84, 1955.
11. Reynolds, L. E.; Brown, C. R.; and Price, P. B.: Effects of Local Chilling in Treatment of Burns, S. Forum **6**:85-87, 1955.
12. Mulholland, J.: Treatment of Burns, Cornell Conferences on Therapy, New York J. Med. **53**:985-992 (April 15) 1953.

Treatment of the Chronically Ill Patient.—Rheumatoid arthritis is the prototype of a chronic disease, with a protracted course of progressive joint inflammation and destruction over many years, finally leaving the patient with severe permanent disability. Although periods of complete bed rest may be necessary during phases of great joint inflammation, this can be avoided or limited to a few weeks in most cases. During bed rest, the danger of crippling flexion contracture of knees and hips, muscle atrophy, and osteoporosis is especially great. The same precautions should be taken as outlined above. Most arthritics may be ambulatory or semiambulatory, some chair-bound. It is still impossible to cure arthritis or permanently to arrest its progress. Steroid hormones and butazolidin act as anti-inflammatory agents during the period of application. Gold therapy is of doubtful value. All these drugs have undesirable or dangerous side effects which cannot always be avoided. Salicylates are moderately good pain relievers. Treatment of arthritis then consists of improving nutrition, and of checking inflammation and pain at least temporarily with the above drugs. Physical therapy and rehabilitation must be constituted as soon as joint inflammation has been brought under tolerable control. It is essential to keep the patient walking and using his hands and shoulders. Active and passive range of motion exercises to all joints several times daily should be given carefully enough to avoid trauma. Resistive exercises on noninvolved joints and muscle setting on involved painful joints help to maintain muscle power. Heat applications relieve pain, relax muscles, and sometimes reduce chronic inflammations. Splints may be required to avoid contractures of knees and elbows. Finger deformities, however, develop in spite of the best care. Spinal braces, knee braces, or walking braces may have to be given for the sake of protection and correction of postural anomalies. Confronted with a chronic progressive and destructive disease, the patient needs moral support. Maintenance of occupation or light housework is very important. Diversional activities are a mediocre substitute for more purposeful and productive activities. The patient should be treated in the home with the aid of family, visiting nurse, or therapist, or be handled on an ambulatory basis. Hospitalization should be a rare exception.—K. Harpuder, M.D., Basic Medical Principles in the Treatment of the Chronically Ill Patient, *Journal of Chronic Diseases*, August, 1956.

AGAMMAGLOBULINEMIA AND HYPOGAMMAGLOBULINEMIA—THE FIRST FIVE YEARS

Beach Barrett, M.D.
and
Wade Volwiler, M.D., Seattle

• *More than 70 case reports have defined congenital agammaglobulinemia and acquired hypogammaglobulinemia as disease entities. These patients present with repeated, severe bacterial infections. They lack normal isohemagglutinins, anti-A and anti-B, and are unable to form antibodies. Serum electrophoretic studies reveal a striking absence of gamma globulin. Definite diagnosis is best made by quantitating gamma globulin immunochemically. Reports indicate that the immunochemically determined concentration of gamma globulin is 0 to 30 mg. per 100 cc. in congenital cases, 0 to 76 mg. in acquired cases, and approximately 1,100 to 2,100 mg. in normal persons. Important considerations in treatment are the prompt control of any existing infection with antibiotics and the prevention of recurrences with maintenance gamma globulin therapy.*

One of the patients here reported on appeared to have acquired hypogammaglobulinemia, except that his level of circulating gamma globulin (200 mg. per 100 cc.) was above that generally accepted for this diagnosis. A second patient developed repeated infections after a diagnosis of multiple myeloma. His serum contained large amounts of gamma myeloma protein, and antigen injections produced only partial responses. In both cases it was decided to withhold gamma globulin therapy because of uncertainties in the diagnosis.

Gamma globulin therapy is painful, expensive, and must be given indefinitely. The authors urge that it not be undertaken without firm proof of the diagnosis.

The newly discovered disease entity called agammaglobulinemia or hypogammaglobulinemia is assuming an important place in medicine. In clinical practice, this diagnosis must be considered whenever a patient has unusually low resistance to bacterial infection. In the laboratory, study of known cases has provided important information in the fields of immunology, hematology, metabolism of plasma proteins, and transplantation of tissue.

Five years ago, Bruton [1] reported the first case of agammaglobulinemia. By 1953, Janeway, Apt, and Gitlin [2] were able to confirm Bruton's findings in nine cases. The continuing search for individuals who are unable to synthesize normal gamma globulins has already resulted in over 70 published case reports.

The clinical finding common to these immunological cripples is an unusual susceptibility to bacterial infection. Many of them have several major bacterial diseases within a few months. Pneumonia, bacteremia, otitis media, and meningitis follow each other with alarming rapidity. Some patients develop chronic bacterial infections, such as bronchiectasis and chronic otitis media. In striking contrast, viral infections are usually handled in a normal fashion with subsequent immunity.[3] A few patients, however, have been reported who had progressive vaccinia, recurrent mumps, or a chronic hepatitis thought to be viral.

Classification of Cases

Individuals reported by others to have very low levels of circulating gamma globulin may be divided into four groups: those with congenital agammaglobulinemia (39 cases reported), those with acquired or adult hypogammaglobulinemia (25 cases reported), those with secondary hypogammaglobulinemia (7 cases reported), and newborn infants with physiological hypogammaglobulinemia. The patients in the first three groups have a prolonged and probably permanent defect of their antibody-producing tissue. The infants in the fourth group have low levels of gamma globulin for a few weeks before they develop their normal ability to synthesize antibodies.

Congenital Agammaglobulinemia.—Complete inability to synthesize gamma globulin from birth is the expression of a sex-linked, Mendelian-recessive genetic defect. Therefore, it is transmitted by women who are otherwise normal to one-half of their male offspring. The family history may reveal that one or more male relatives either have the same defect or have died of overwhelming bacterial infection early in life. The patient usually has the first of a series of severe bacterial infections soon after he reaches 6 months of age. By that time, he has metabolized completely the supply of gamma globulin received from his mother in utero. In the preantibiotic era, these children doubtless died of their first or second bout of pneumonia or meningitis.

Acquired Hypogammaglobulinemia.—Patients who lose the ability to synthesize gamma globulin later in life differ in several respects from those with the congenital form of the disease. Either males or females are afflicted. The history does not reveal any familial tendency toward this disorder. During their early years of life, these individuals handle bacterial disease successfully. Then, for an unknown reason, they suddenly lose the ability to form antibodies and, as a result,

From the Department of Medicine, University of Washington School of Medicine. Dr. Barrett is an A. H. Robins Research Fellow.

Read before the 10th Clinical Meeting of the American Medical Association, Seattle, Nov. 30, 1956.

suffer a series of bacterial infections. Whether this failure of antibody production is caused by the first severe infection or whether it arises as a late expression of a congenital defect is not known.

Secondary Hypogammaglobulinemia.—The third group consists of those patients who develop hypogammaglobulinemia because some diffuse disease of the reticuloendothelial system interferes with the production of antibodies by normal plasma cells. Leukemia,[4] lymphoma, and myeloma [5] are diseases that occasionally cause this paralysis of the immune mechanism. Other possible causes of secondary hypogammaglobulinemia include total body irradiation and therapy with mechlorethamine hydrochloride (nitrogen mustard).

Physiological Hypogammaglobulinemia.—When the levels of serum gamma globulin were measured in a group of infants from 2 to 4 months of age, it was observed that most of them had levels of approximately 300 mg. per 100 cc. and that a few had levels as low as 150 mg. per 100 cc.[6] This is far below the normal adult range of from 1,100 to 2,100 mg. per 100 cc., as determined by an immunoprecipitin technique.

Figure 1 presents the probable explanation for this transient depression of the level of serum gamma globulin: The normal human infant is born with a level of approximately 1,000 mg. per 100 cc. of serum gamma globulin, all of which was either transferred from the mother or produced by the placenta. This passively acquired gamma globulin is metabolized in a normal fashion, one-half of the amount being catabolized each 28 days.[7] By the fourth month, very little maternal gamma globulin remains in the infant's circulation.

The fetus and newborn infant are apparently unable to synthesize gamma globulin, but, as the reticuloendothelial system matures and the infant is challenged by various antigens, production gradually begins. Most infants then produce enough gamma globulin to keep their total serum concentration from falling below 300 mg. per 100 cc. In a few production is slow in starting, and, therefore, the total level falls lower. In all normal infants adult levels of gamma globulin are approached by one year of age.

In no extensive study have the transiently low levels of gamma globulin at from 2 to 4 months of age been correlated with a high incidence of bacterial disease, although it seems likely that such a correlation exists.[6] This period may be particularly hazardous for premature infants who begin life with significantly lower levels of gamma globulin than do normal infants. The possible physiological dip in the level of gamma globulin requires that a final diagnosis of congenital agammaglobulinemia be deferred until a child is over 8 months of age.

From the foregoing classification, it is evident that case finding cannot be restricted to one sex or one age group. Any patient exhibiting strikingly poor resistance to bacteria should be screened for hypogammaglobulinemia.

Laboratory Studies

Presumptive Tests.—Certain common laboratory tests usually reflect the hypogammaglobulinemic state. Although the following tests have been found to be helpful in the diagnosis, they do not definitely confirm or rule out the disease.

Concentration of Total Serum Globulins: When the total globulin concentration in normal serum is measured by routine salting-out methods, nearly one-half of the reported concentration is gamma globulin. Therefore, hypogammaglobulinemia will cause an abnormally low level of total globulin provided the other components of the globulin fraction are not elevated by chronic disease. The following total globulin concentrations were reported in 32 patients: from 0.4 to 1.0 Gm. per 100 cc. in 16 patients, from 1.1 to 2.0 Gm. per 100 cc. in 11 patients, and from 2.0 to 2.7 Gm. per 100 cc. in 5 patients.

Isohemagglutinin Titers: The titer of isohemagglutinins, anti-A or anti-B, gives an important evaluation of the immune mechanism. A normal person who is not of type AB and who is over 2 years of age usually has a titer of anti-A or anti-B of 1:8 or higher. A low or absent isohemagglutinin titer strongly suggests

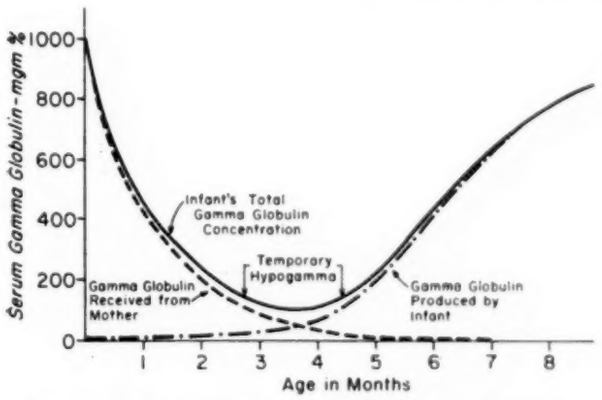


Fig. 1.—Graph showing levels of gamma globulin in physiological hypogammaglobulinemia of newborn infants. As level of gamma globulin from mother drops and production by infant begins, there is a temporary drop in gamma globulin concentration.

hypogammaglobulinemia, whereas a high titer probably rules out the disease. The following isohemagglutinin titers were reported in 47 patients: absent in 37 patients, from 1:2 to 1:5 in 7 patients, 1:8 in 2 patients, and "normal" in 1 patient.

Response to Antigen Stimulation: Ability to synthesize specific antibody may be evaluated by injecting antigens such as typhoid and diphtheria vaccines. A good antibody response, as measured by Gruber-Widal reaction and the Schick test, tends to rule out hypogammaglobulinemia. These antigens may produce weak responses or none in some otherwise normal individuals. The following responses to antigens in proved cases of hypogammaglobulinemia have been recorded: There was no response to typhoid vaccine in 20 patients, and response was weak in 3. There was no response to diphtheria vaccine in 19 patients, and response was weak in 1.

Zinc Sulfate Turbidity Test: The turbidity test of Kunkel [9] gives a semiquantitative estimate of the concentration of gamma globulin in the serum. An abnormally low value of zero or 1 unit is compatible with the diagnosis of severe hypogammaglobulinemia, while a normal or elevated concentration rules out hypogammaglobulinemia. The results of this test have been reported in very few cases of hypogammaglobulinemia, those levels being zero or 1 unit.

Definitive Tests.—Two definitive tests for hypogammaglobulinemia are electrophoresis of serum and immunochemical quantitation.

Electrophoresis of Serum: Both free and paper electrophoresis of serum provide valuable estimates of the concentration of serum gamma globulin. Paper electrophoresis (fig. 2) is one of the most reliable screening tests for hypogammaglobulinemia. If a

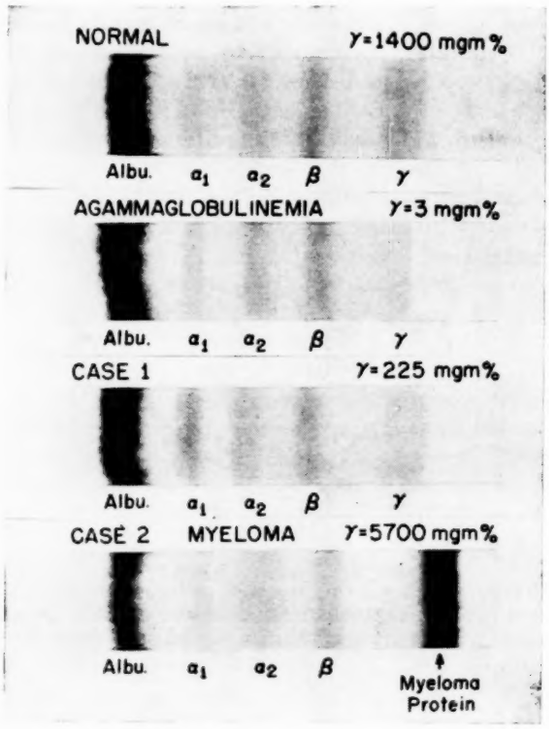


Fig. 2.—Paper electrophoresis of serum specimens showing examples of varying concentrations of gamma globulin encountered in cases of hypogammaglobulinemia. Quantitative values shown were obtained by immunoprecipitin method. Patient in case labeled "Agammaglobulinemia" has congenital syndrome.

normal or nearly normal gamma globulin band is seen on the strip, hypogammaglobulinemia is ruled out; if the band is very faint, the presence of the disease is likely and further confirmation by immunochemical quantitation is indicated.

Immunochemical Quantitation: Immunochemical methods offer the only satisfactory means of sensitively measuring low concentrations of gamma globulin. The best of these techniques appears to be the precipitin method,[10] which involves the quantitative analysis of the precipitate formed between the serum to be tested and a specific antiserum to human gamma globulin developed in rabbits, goats, sheep, horses, or chickens. At present, this method is available in few medical research centers. An alternate immunological method is the erythrocyte agglutination-inhibition test as employed by Wiener [11] and Grubb [12]; this method appears to be satisfactory for diagnosis but less precise for measuring exact concentrations of gamma globulin.

The normal concentration of gamma globulin, determined immunochemically, found in the serums of adults has not been well documented. Preliminary studies in the laboratory of the University of Washington School of Medicine with the precipitin technique using antigamma rabbit serum indicate that normal concentration of gamma globulin probably varies from 1,100 to 2,100 mg. per 100 cc. Such values vary somewhat with the method for analyzing antigen-antibody precipitates,[10] with the kind of gamma globulin used as antigen in preparing antiserum, and with the animal species in which test antiserum is produced. In the few cases of severe hypogammaglobulinemia for which such immunochemical measurement have been reported by others, the following pretreatment levels were found: In 21 cases of congenital agammagobulinemia levels were from 2 to 30 mg. per 100 cc.; in 6 cases of acquired hypogammaglobulinemia levels were from 11 to 76 mg. per 100 cc.

Preliminary experience with replacement therapy suggests that the serum level should be maintained above 150 mg. per 100 cc. in order to give reasonable protection against bacterial infection.[13]

Report of Cases

The following two case reports represent striking examples of the major problems encountered in the diagnosis and treatment of adult hypogammaglobulinemia.

Case 1 (acquired hypogammaglobulinemia).—A husky, 19-year-old sailor contracted pneumonia twice within two months. His family and personal history revealed no unusual susceptibility to bacterial disease. Laboratory studies included a total serum protein level of 6.2 Gm. per 100 cc., of which 1.6 Gm. was globulin. The patient's blood type was A, but there were no anti-B agglutinins in his serum.

Paper electrophoresis of the serum (fig. 2) revealed normal bands for all major protein components except gamma globulin, the band of which was markedly reduced. Immunoquantitative analysis of gamma globulin gave values that ranged irregularly from 170 to 250 mg. per 100 cc. over a period of several months. Injections of typhoid vaccine failed to produce a Gruber-Widal reaction. The patient was observed for 10 months. Therapy with gamma globulin was not given because he had no further infections.

The levels of gamma globulin in the serums of patients with acquired hypogammaglobulinemia reported by others have varied from 11 to 70 mg. per 100 cc. by immunochemical methods. The values for this patient lie precariously on the borderline between dangerous hypogammaglobulinemia and "safe," though definite, hypogammaglobulinemia.

When a patient, such as the one in the case reported above, has unusual susceptibility to infection, poor antibody responses, and a serum level of gamma globulin consistently in the range of 200 mg. per

100 cc., it is difficult to decide whether to start replacement therapy or to await further developments. Fortunately, it was possible to keep the patient under close observation for many months. When no further infections occurred, he was returned to military duty with instructions to report for medical attention at the first sign of recurrent infection. It is our belief that this case represents an example of acquired adult hypogammaglobulinemia in which the depression of the synthesis of gamma globulins is not quite so severe as is usually found in this condition.

Case 2 (multiple myeloma).—A 67-year-old man was given a diagnosis in March, 1956, of multiple myeloma. At that time he complained of generalized weakness and pain in his bones. Laboratory study revealed a hematocrit of 16%, total serum globulin level of 6.3 Gm. per 100 cc., a typical paraprotein band on serum paper electrophoresis, and marrow aspirate with malignant plasma cells and suppresion of normal cellular elements.

The patient could recall no significant infections prior to the diagnosis of myeloma. Beginning one month after this diagnosis was established, the following infections were observed: on April 2, 1956, bronchopneumonia (gram-positive cocci in sputum); on April 18, 1956, otitis media (no organism recovered); on May 8, 1956, pneumonia in right lower lobe (no organism recovered); on May 17, 1956, abscess at site of venipuncture (no organism recovered); on May 30, 1956, abscess in opposite arm (no organism recovered); on Sept. 29, 1956, pneumonia in right lower lobe (no organism recovered); on Dec. 2, 1956; bronchopneumonia (a few pneumococci in sputum); on Jan. 2, 1957, pneumonia in right lower lobe (no organism recovered); and on Feb. 18, 1957, pneumonia in right upper lobe (pneumococci in sputum). Each of the above infections responded well to antibiotic therapy.

In addition to the persistent anemia due to marrow failure, which required repeated transfusions, the patient exhibited a leukopenia even while acutely ill, with white cell blood counts ranging from 1,600 to 4,500 per cubic millimeter and normal differential counts.

Careful inspection of the serum electrophoretic pattern (fig. 2) revealed an intense paraprotein band characteristic of multiple myeloma located in the gamma-2 position and no apparent protein in the remainder of the gamma globulin region. According to Porges,[14] such an electrophoretic pattern strongly suggests a state of secondary hypogammaglobulinemia. Additionaly, the impressive proof of rapidly recurring infection would seem to indicate the patient's inability to form antibacterial antibodies.

A series of injections with typhoid antigen failed to produce any typhoid agglutinins. However, it was observed that the patient's anti-A isohemagglutinin titer was 1:16, which is higher than that in most reported cases of hypogammaglobulinemia. One week after the intracutaneous injection of 0.2 ml. of purified A substance, this titer rose to 1:1,000, where it remained for several weeks. Immunochemical quantitation of the serum gamma globulin gave a value of over 5,000 mg. per 100 cc., illustrating that the gamma myeloma protein could not be separated immunologically from normal gamma globulins.

There can be no doubt that this patient concurrently developed generalized myelomatosis and extreme susceptibility to infection. The question arises as to whether it was the loss of antibody production or of leukocyte production or the failure of some other defense mechanism that was responsible for the recurring infections. The striking rise in anti-A isohemagglutinins after an injection of purified A substance demonstrated that the patient had an excellent capacity to make at least one type of antibody. Whether this finding completely rules out antibody "immunological paralysis" in this patient is not clear.

Treatment

The two most important considerations in the treatment of a patient who is unable to produce antibodies are (1) the rapid control of acute infections and (2) the prevention of recurrent infection. Experience of others indicates that acute bacterial infection in these patients responds well to antibiotic therapy and that injections of gamma globulin generally do not alter the course of an acute disease. Such failure of pooled human gamma globulin to modify the course of an established infection would be expected because it does not provide enough specific antibody to a single bacterial pathogen. On the other hand, regular injections of gamma globulin may greatly reduce the incidence of reinfection. This treatment seems to offer considerable protection for patients with hypogammaglobulinemia if it is initiated before bacterial infections have caused irreversible tissue damage.

The principles of replacement therapy with pooled human gamma globulin are shown in figure 3. A large initial dose is given to raise the circulating gamma globulin from the very low pretreatment level to a serum concentration well above 150 mg. per 100 cc.,

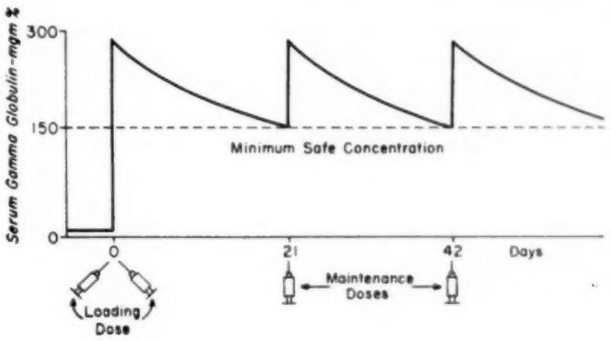


Fig. 3.—Graph showing treatment of agammaglobulinemia with injections of gamma globulin.

which is considered the minimum safe level. Normal catabolism of this added gamma globulin progressively reduces the serum concentration to 150 mg. per 100 cc. in from three to four weeks; at this time and every two to five weeks thereafter, a repeat injection should be given.

Most such patients can be kept reasonably free of bacterial infection by the giving of injections of from 100 to 150 mg. of pooled human gamma globulin per kilogram of body weight every two to four weeks,[8a] but others may require higher serum gamma globulin levels.[13] These intramuscular injections are large, painful, and expensive, and they should be given on a regular schedule for an indefinite period. Such heroic therapy should never be undertaken without firm proof of the diagnosis. An immunochemical determination of the concentration of gamma globulin should be made before treatment is started. This determination should be repeated occasionally just prior to the administration of a maintenance injection in order to establish the adequacy of the treatment schedule.

Prognosis

The prognosis in these patients awaits further years of study. A disturbing note has been the development of a peculiar hydrarthrosis of the knees in some of the patients with the congenital form of the disease who have been treated for several years.[15] It is thought that this represents a reaction to repeated infection rather than a result of gamma globulin therapy. In spite of therapy, there is a constant danger from infectious disease, and existence is perilous at best for this group.

Comment

Study of individuals with hypogammaglobulinemia has raised fundamental questions concerning resistance to infectious disease. Of particular interest is the observation that bacterial infections are such a major problem, while viral infections are generally contracted only once with subsequent immunity. Circulating antibodies are only one of several factors necessary to specific immunity. One may theorize that circulating antibodies are more important for immunity to bacterial disease, while as yet poorly defined tissue factors are more important for immunity to viruses. Such differentiation is not complete, as there have been instances of repeated viral infections, of progressive vaccinia, and of fatal viral hepatitis among patients with agammaglobulinemia. On the other hand, it has been observed that most of these patients have one ordinary bout of measles, mumps, or chicken pox and are thereafter immune.[3]

In an attempt to discover why these patients lack gamma globulin, the life span of injected gamma globulin in their circulation has been measured. The evidence thus far indicates that administered gamma globulin circulates in these patients as long as it does in normal persons,[8a] indicating that the basic defect is failure to synthesize gamma globulin rather than abnormally rapid destruction or loss. Hematological studies have demonstrated that plasma cells are either extremely scarce or absent altogether from the lymphatic tissues and bone marrow of these patients and that antigenic stimulation fails to produce a proliferation of plasma cells as it does in the normal subject.

There is increasing evidence that the rejection of tissue transplants is an immunological phenomenon. It follows that a person with immunological paralysis might accept a tissue graft from an unrelated donor. Indeed, such skin grafts have been successfully applied to two patients with agammaglobulinemia,[16] and these grafts have survived for many months and have been definitely accepted. This is in sharp contrast to the observation that normal individuals always reject grafts from unrelated donors.

Summary

Five years of case finding and study in the United States have given preliminary understanding of an unusual and important new disease entity. While proved cases are scarce, the number of patients who suffer from repeated bacterial infection and who should be studied for hypogammaglobulinemia is large. Each correct diagnosis is of great importance to the patient, who will benefit from rational treatment, and to the medical world for further fundamental understanding of the basic immune mechanism.

This study was supported by research grants from the Institute of Arthritis and Metabolic Diseases of the National Institutes of Health, Public Health Service, and from the A. H. Robins Company, Inc., Richmond, Va.

Dr. Eloise Giblett, King County Central Blood Bank, supervised the determination of isohemagglutinin titers.

The patient in case 1 is reported with permission of Drs. Emanuel Rollins, A. F. Hilfer, and R. F. Schugmann, U. S. Naval Hospital, Bremerton, Wash.

References

1. Bruton, O. C.: Agammaglobulinemia, Pediatrics **9:**722-727 (June) 1952.

2. Janeway, C. A.; Apt, L.; and Gitlin, D.: "Agammaglobulinemia," Tr. A. Am. Physicians **66:**200-202, 1953.

3. Good, R. A., and Zak, S. J.: Disturbances in Gamma Globulin Synthesis as "Experiments of Nature," Pediatrics **18:**109-149 (July) 1956.

4. Jim, R. T. S., and Reinhard, E. H.: Agammaglobulinemia and Chronic Lymphocytic Leukemia, Ann. Int. Med. **44:**790-796 (April) 1956.

5. Zinneman, H. H., and Hall, W. H.: Recurrent Pneumonia in Multiple Myeloma and Some Observations on Immunologic Response, Ann. Int. Med. **41:**1152-1163 (Dec.) 1954. Lawson, H. A., and others: Observations on Antibody Content of Blood in Patients with Multiple Myeloma, New England J. Med. **252:**13-18 (Jan. 6) 1955.

6. Orlandini, T.; Sass-Kotsak, A.; and Ebbs, J. H.: Serum Gamma Globulin Levels in Normal Infants, Pediatrics **16:**575-584 (Nov.) 1955.

7. Volwiler, W., and others: Biosynthetic Determination with Radioactive Sulfur of Turn-over Rates of Various Plasma Proteins in Normal and Cirrhotic Man, J. Clin. Invest. **34:**1126-1146 (July, pt. 1) 1955; Unpublished data.

8. (*a*) Janeway, C. A., and Gitlin, D.: Gamma Globulins, in Advances in Pediatrics, edited by S. Z. Levine, Chicago, Year Book Publishers, Inc., 1957, vol. 9, pp. 65-136. (*b*) Good, R. A.; Varco, R. L.; Aust, J. B.; and Zak, S. J.: Transplantation Studies in Patients with Agammaglobulinemia, Ann. New York Acad. Sc. **64:**882-924 (March 22) 1957.

9. Kunkel, H. G.: Estimation of Alterations of Serum Gamma Globulin by Turbidimetric Technique, Proc. Soc. Exper. Biol. & Med. **66:**217-224 (Oct.) 1947.

10. McDuffie, F. C., and Kabat, E. A.: Comparative Study of Methods Used for Analysis of Specific Precipitates in Quantitative Immunochemistry, J. Immunol. **77:**193-197 (Sept.) 1956.

11. Wiener, A. S.: Serologic Test for Human Gamma Globulin: II. Application in Diagnosis and Treatment of Agammaglobulinemia, Am. J. Clin. Path. **25:**595-597 (May) 1955.

12. Grubb, R.: Method for Demonstrating Minute Amounts of Human γ-Globulin, Acta path. et microbiol. scandinav. **38:**339-346, 1956.

13. Martin, C. M.; Gordon, R. S.; and McCullough, N. B.: Acquired Hypogammaglobulinemia in an Adult: Report of Case, with Clinical and Experimental Studies, New England J. Med. **254:**449-456 (March 8) 1956. Footnote 8*a*.

14. Porges, R. F.: Method for Demonstrating Secondary Agammaglobulinemia in Patients with Multiple Myeloma, Using Paper Electrophoresis, J. Lab. & Clin. Med. **47:**960-968 (June) 1956.

15. Janeway, C. A.; Gitlin, D.; Craig, J. M.; and Grice, D. S.: "Collagen Disease" in Patients with Congenital Agammaglobulinemia, Tr. A. Am. Physicians **69:**93-97, 1956.

16. Good, R. A., and Varco, R. L.: Successful Homograft of Skin in Child with Agammaglobulinemia, J. A. M. A. **157:**713-716 (Feb. 26) 1955.

CLINICAL NOTES

FOCAL ENCEPHALOPATHY AFTER ADMINISTRATION OF TETANUS ANTITOXIN

Charles M. Poser, M.D., Kansas City, Kan.

The purpose of this communication is to report an instance of the focal cerebral type of complication after tetanus antitoxin administration. Since the discovery of antibiotics and chemotherapeutic agents, the use of immune serums has almost been abandoned in medical practice, and thus reactions caused by hypersensitivity to rabbit or horse serum have become relatively rare. There remains, however, one preparation in fairly common use which does give rise to serum reactions: tetanus antitoxin. Serum sickness after its administration is not infrequent and, according to Rackemann,[1] occurs in approximately 30% of all patients who have received the serum.

The neurological complications which may follow or accompany serum reactions are of different types. The most commonly described is the so-called serum neuritis occurring after the administration of tetanus antitoxin. This usually takes the form of a brachial neuritis, with particular involvement of the fifth and sixth cervical roots, but may affect other peripheral nerves and trunks, such as the ulnar, the median, or the sciatic nerves. A less frequent variety is a diffuse encephalomyelitic type and a generalized polyneuropathy resembling the Guillain-Barré type or acute ascending myelitis (Landry's paralysis). Finally, the rarest of all forms is the focal cerebral type.

Report of a Case

A 41-year-old housewife was admitted to the neurology service of the University of Kansas Medical Center on April 17, 1956, with the chief complaint of weakness of the left side of the body and face. On April 11, the patient suffered a laceration of the left side of the forehead which resulted from mild trauma suffered within her home. She received 1,500 units of tetanus antitoxin after a negative skin test. The laceration was sutured, and she returned home. On April 15, she complained of "feeling cold," and the next day she noted aching in her muscles and occasional chilly sensations. On the evening of April 17 angioneurotic edema (giant urticaria) appeared and covered her whole body. Her eyes swelled shut, and she complained of severe itching of the scalp. She was given an unknown amount of diphenhydramine hydrochloride, which relieved the swelling and caused the edema to disappear. On April 19, she became unable to urinate even though she felt the urge to do so. A few hours later she had difficulty in moving her left leg, and over a period of several hours she noted paresthesias in her left arm and leg and increasing weakness of these extremities.

The history is of interest in that the patient had had an allergic reaction to penicillin approximately one year previously. At about that time, during her 15th pregnancy, she had neuropathy of the facial nerve (Bell's palsy) on the left side, which disappeared in approximately six weeks without leaving any residuum. The patient stated that she has "asthma" every spring, usually associated with "sinus trouble," a chronic cough productive of large quantities of mucus-like material, and occasional wheezing.

From the Department of Medicine (Neurology), University of Kansas School of Medicine.

Physical examination revealed a well-nourished, well-developed woman who seemed to be in mild distress. Her temperature on admission was 98.6 F (37 C), her pulse rate was 102 beats per minute, and her blood pressure was 112/80 mm. Hg. The patient was drowsy but easily aroused, well oriented, and cooperative. The neck was supple. The cranial nerves showed no abnormalities except for a mild left-central type of facial weakness. The optic fundi were not remarkable, and the patient had no difficulty with speech, swallowing, or respiration. There was moderately severe hemiparesis of the left which was slightly more pronounced in the upper extremity. Reflexes on the left side were hyperactive compared with those on the right. The plantar reflex on the left side was extensor, while that on the right side was equivocal. There were perceptible hypesthesia and hypalgesia in the entire left side of the body except the face. In addition, the muscles of the right side had occasional tonic spasms, especially those of the right leg. The patient perspired profusely but only on the left side of her face and body.

Cerebellar function tests were all performed well. The general physical examination was not remarkable except that the patient's bladder was percussed to approximately the level of the umbilicus. The patient stated that she had not voided for approximately 24 hours. The laboratory findings are summarized in the table.

Course in the Hospital.—The patient remained very drowsy for the first few hours. During this period of time the deep tendon reflexes on the right side became noticeably hyperactive, and the plantar reflex was definitely abnormal. The tonic spasms in the right leg grew more frequent and became painful to the patient. On the evening of the day of admission, administration of 25 mg. of cortisone and 500 mg. of zoxazolamine was started three times a day, after the patient had received a total of 20 U. S. P. units of corticotropin (ACTH) intravenously. The next morning the patient said her muscle cramps had completely disappeared and that the tonic spasms were absent thereafter. She was placed on a salt-poor diet, and administration of 1 Gm. of potassium chloride three times a day was added to the regimen. On the following morning, April 22, the patient was still drowsy and appeared apprehensive. She continued to have difficulty in initiating micturition, although she was able to void spontaneously. During the night she slept fitfully, awakening at frequent intervals. She was well oriented and responded to questions, but she remained drowsy. Her speech was slightly slurred but was intelligible. She was incontinent of urine on several occasions.

On April 23, the patient still seemed lethargic. Because she continued to have difficulty in voiding, a catheter was inserted. Her speech was still somewhat slurred, and long periods of conversation seemed to exhaust her and render her breathless. On April 24, she seemed more alert but was confused on awakening the morning of the next day. She continued to be drowsy and slept most of the day. On April 26, the patient was slightly disoriented, but she answered questions rationally. By April 27, her sensorium had cleared; she was much more alert, not sleeping as much as before, and was almost back to normal. Even though there was complete paralysis of the left arm, she was now able to raise her left knee slightly.

From that point on the patient remained alert and improved slowly but progressively. By the time of her discharge, she was able to walk again with the use of a cane, while function returned much more slowly in the left arm and consisted only of slight abduction and adduction of the left shoulder. By May 4, the catheter was removed, and the patient was able to void spontaneously and without difficulty. Disturbance in perspiration continued, and by the time of the patient's discharge

perspiration was much more profuse on the left side of the face and body than it was on the right side. She was afebrile for the entire period of hospitalization. At no time did she complain of headache or stiff neck. Electroencephalograms were taken at regular intervals throughout the patient's hospitalization and originally revealed a distinct right temporal slow-wave focus superimposed on a generalized disorganization. This cleared to some degree, and the focus became less well defined in subsequent tracings.

Comment

The central nervous system involvement appears to be of a generalized encephalomyelitic type, but the hemiparesis of the left side and hemisensory defect suggest an additional focal vascular lesion of the right frontal lobe. Serial electroencephalographic tracings tend to confirm this impression, but, on the other hand, the patient's mental state during the acute phase of the disease and the transient weakness of convergence are more indicative of a diffuse lesion of the upper brain stem. The rather severe spasticity of the right side of the body and the lack of perspiration on that side indicate that the upper cervical segments or brain stem were affected. It is difficult to explain the absence of Horner's syndrome when postulating that the lack of sweating of the entire right side of the body, including the face, resulted from the disease of the intermediolateral horn on the ipsilateral side.

Park and Richardson [2] have recently published an excellent review of the cerebral complications of serum sickness in which they stress the rarity of the focal type of involvement. In addition to their own two cases, they were able to collect only nine additional instances of that type from the literature, two of which were published in the United States. In seven of the cases the patients had received tetanus antitoxin; in two, scarlet fever antitoxin; and in the last two, diphtheria antitoxin. The cases were all characterized by a rather sudden onset of hemiplegia accompanied by confusion, coma, or convulsions. Park and Richardson considered this compatible with a lesion resulting from vascular occlusion or insufficiency.

Rich [3] has suggested that the collagenous tissue of the media of the arterial wall is the site of the antigen-antibody reaction and that anaphylactic injury to the endothelium and media may result in edema, sufficient in itself to occlude the vessel or impair circulation through it, or lead to increased permeability and even necrosis of the vessel wall. In addition to damage to arterioles, which the lesion in this case suggests, scattered lesions may give rise to a more diffuse involvement which is reminiscent of the perivenous swelling, demyelinization, and eventual gliosis seen in the so-called postexanthematous encephalomyelitis and the postvaccinal encephalomyelitis. In these two types of encephalomyelitis, an allergic type of reaction has also been postulated.

Rutstein and co-workers [4] found that 31% of patients receiving rabbit antipneumococcic serum had allergic reactions but that this increased to 45% among patients with known histories of allergy. It is important to point out in this case that there was a history of previous allergies: The patient had "asthma" characterized by wheezing and a cough productive of large amounts of sputum. She had had an allergic reaction to an injection of penicillin and an unexplained peripheral facial nerve palsy during her last pregnancy.

The presence, initially, of 39 white blood cells, with 90% lymphocytes, in the cerebrospinal fluid is suggestive of an acute inflammatory reaction. It is also possible that it represented a mild degree of meningitis, as reported by Walsh.[5] The subsequent slight increase in total amount of protein is also compatible with resolution of such a process and the occurrence of a process occasionally seen in poliomyelitis, where a delayed rise in the amount of protein in the cerebrospinal fluid usually takes place after the cells have disappeared. The serum electrophoretic pattern, with an increase in the alpha-2 globulin value, is compatible with an acute inflammatory process. The heterophil agglutination was positive in a dilution of 1:224, and two weeks later it was down to 1:112. Absorption with guinea-pig kidney and beef erythrocytes was negative on both occasions. This type of reaction corresponds to what Stuart and co-workers [6] described in serum sickness. The slight changes in the liver-function tests, which showed a decrease in thymol turbidity, a rise in serum albumin, a fall in serum globulin, and a rise in both total cholesterol and cholesterol esters, are difficult to interpret since these functions were not abnormal to begin with.

Laboratory Findings for Patient with Focal Encephalopathy After Administration of Tetanus Antitoxin *

Date, 1956	Hb., Gm./ 100 Cc.	WBC/ Cu. Mm.	ESR, Mm./Hr.	Heterophil Agglutination Ratio	Serum Albumin, Gm./ 100 Cc.	Serum Globulin, Gm./ 100 Cc.	Thymol Turbidity, Units	Cephalin Flocculation	Total Cholesterol, Mg./ 100 Cc.	Cholesterol Esters, %	CSF WBC/ Cu. Mm.	CSF Total Protein, Mg./ 100 Cc.	Colloidal Gold Curve
4/21											39	62	001211100
4/22	12.2	9,900											
4/23			22	1:224†	4.61	2.04	7	Neg.	186	61			
4/24											2	52	000111000
5/1											1	75	000110000
5/3	14.3	14,500		1:112‡									
5/7	13.9	13,100	18		4.94	1.86	6	Neg.	214	69			
5/8	14.1	11,900	20										
5/11	14.3	10,450									2	68	001110000
5/21			23										
5/22	15.2	10,300											
5/23											3	55	012100000

* Serum electrophoresis on April 23 and May 22 revealed increased alpha-2 globulins. Urinalyses, blood and cerebrospinal-fluid serology, and skull and chest x-rays were negative. Blood values were as follows: fasting sugar, 100 mg.; nonprotein nitrogen, 38 mg.; calcium, 5.1 mg.; and phosphorus, 1.9 mg. per 100 cc.

† Guinea-pig kidney absorption, 1:14.

‡ Guinea-pig kidney absorption, 1:7; beef erythrocyte absorption, negative.

It is not easy to evaluate the efficacy of the corticotropin-cortisone therapy in this case. Walsh [5] felt that his patient did not profit from 10 days' daily administration of 100 mg. of cortisone intramuscularly, since the course of his illness did not differ from that of other patients who had not received cortisone. However, the well-recognized value of cortisone in generalized acute allergic reactions prompted me to use steroid therapy, and it is my belief that the therapy may have been responsible, at least in part, for the rather short duration of the drowsiness and irritability displayed by the patient during the early stage of the disease.

The injury for which the patient had been given tetanus antitoxin was a laceration of the forehead incurred by bumping her head against the door of a kitchen cabinet. She was duly skin-tested before tetanus antitoxin injection, and the test was noted to be negative. As the chances of contamination with Clostridium tetani were remote at best, there seems to have been no need for administering antitetanic serum. The fact that the skin test was negative did not necessarily indicate the absence of a generalized hypersensitive state.

Serum sickness is usually a benign illness, but its neurological complications, although not fatal, may result in severe disability. Prevention of such complications would be helped by carefully considering the need for tetanus prophylaxis and using tetanus toxoid whenever possible. In cases in which the indications for the use of tetanus antitoxin are clear, inquiry concerning the previous history of allergy may provide, if positive, reasons for administering the serum in divided, gradually increasing doses even in the absence of a positive skin reaction.

Summary and Conclusions

In a case of neurological complication that was due to the administration of tetanus antitoxin, a focal type of cerebral involvement suggesting a vascular lesion, with hemiparesis of the left side, was superimposed on what was probably a rather diffuse encephalomyelitis. Treatment with corticotropin (ACTH) and cortisone apparently helped hasten partial recovery. In this case no clear indication for the use of tetanus antitoxin existed at the time of the original injury. In view of the possible serious neurological consequences, a plea is made for reexamining the routine practice of administering antitetanus prophylaxis.

References

1. Rackemann, F. M.: Medical Progress: Allergy: Serum Reactions with Particular Reference to Prevention and Treatment of Tetanus, New England J. Med. **226:**726-733 (April) 1942.

2. Park, A. M., and Richardson, J. C.: Cerebral Complications of Serum Sickness, Neurology **3:**277-283 (April) 1953.

3. Rich, A. R.: Hypersensitivity in Disease, Harvey Lectures, 1946-1947, Springfield, Ill., Charles C Thomas, Publisher, series 42, p. 106.

4. Rutstein, D. D.; Reed, E. A.; Langmuir, A. D.; and Rogers, E. S.: Immediate Serum Reactions in Man: Classification and Analysis of Reaction to Intravenous Administration of Antipneumococcus Horse Serum in Cases of Pneumonia, Arch. Int. Med. **68:**25-56 (July) 1941.

5. Walsh, J. W.: Peripheral Neuropathy and Serous Meningitis Due to Horse Serum: Report of Case with Failure to Respond to Cortisone, New England J. Med. **247:**88-91 (July 17) 1952.

6. Stuart, C. A.; Welch, H.; Cunningham, J.; and Burgess, A. M.: Infectious Mononucleosis: Further Studies, Arch. Int. Med. **58:**512-522 (Sept.) 1936.

The Nutrition of Isolated Cells.—There are in the body a great many different sorts of "epithelium." The skin is largely a protective layer and as such is thickened, keratinized. The lining of the intestine is a secretory layer as well as an absorptive one, and, as such, keratinization would interfere with its function. It is, rather, a simple columnar epithelium of glandular cells. Still a third type occurs in the lungs and nasal mucosa, where secretory function is coupled with a mechanical role in the ciliated layers. The cells originating in these three layers can all be grown in tissue culture, and if they are maintained in the usual nutrients they will all eventually take on a pattern resembling the intestinal cells. But if they are nourished with serum taken from animals, usually birds, which have been reared on a low vitamin A diet, so that they are deficient in this respect, the secretory function regresses and keratinization sets in. If, on the other hand, the serum is artificially fortified with excessively high vitamin A levels, there will be first a marked development of secretory function under the keratinized layers, these latter will be sloughed off, and eventually certain cells will develop active cilia, as well as accumulating mucous. The type of epithelium developed is thus sharply dependent on the amount of vitamin A available to the cells. The particular morphology of a given organ may be determined by the distribution of such substances in the body. At this level, at least, specific cell type is not internally but externally determined. The same holds true for bone. An excised femur can be caused to disintegrate into an amorphous mass of quite healthy chondroblasts without a trace of ossification, merely by increasing the level of vitamin A available to it. "Optimal" nutrition can obviously be a very specific and highly localized affair! Unfortunately, this work of Fell and Mellanby has only opened for us a tiny window into the vaults and chambers of nutritional morphogenesis. Vitamin A just happens to be one of the few substances for which we have recognized a specific formative function and which can at the same time be successfully manipulated in the simple fashion required by our present rather crude techniques. I am sure that there are many, many others.—P. R. White, Ph.D., The Nutrition of Isolated Cells from Vertebrates, *The American Journal of Clinical Nutrition*, November-December, 1956.

COUNCIL ON DRUGS

Formerly the Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL DRUGS

Formerly New and Nonofficial Remedies

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations. Applicable commercial names for preparations of evaluated drugs are listed at the end of monographs and parenthetically in the text of supplemental statements; additional commercial names of which the Council is informed will be included with subsequently published supplemental statements and annual editions of New and Nonofficial Drugs.

H. D. KAUTZ, M.D., *Secretary.*

Mumps Skin Test Antigen.—A sterile suspension of killed mumps virus in isotonic sodium chloride solution, preserved with 1:10,000 thimerosal. The virus is grown in embryonated chicken eggs and is inactivated by ultraviolet light or formaldehyde. Mumps skin test antigen is tested for antigenicity, sterility, and safety according to specifications of the National Institutes of Health. Each cubic centimeter contains 20 complement-fixing units.

Actions and Uses.—Mumps skin test antigen is used to detect specific skin hypersensitivity to the mumps virus. Thus, it may be employed to determine susceptibility to mumps or to confirm a tentative diagnosis of the disease. The development of skin sensitivity seems to require some time. Confirmation of a tentative diagnosis of mumps can be achieved only several weeks to months after onset of the disease. The skin test antigen generally should be used prior to vaccination in order to identify suitable nonimmune candidates for active immunization. Use of mumps vaccine or repeated skin tests do not seem to affect the skin reaction. Since mumps skin test antigen is prepared from the embryonic fluid of chicken eggs, its administration is absolutely contraindicated to persons giving a history of hypersensitivity to egg, chicken, or chicken feathers. If there is a negative history of hypersensitivity and a pseudo-positive reaction indicating hypersensitivity develops from a skin test, subsequent use of mumps vaccine is contraindicated.

Dosage.—Mumps skin test antigen is administered intradermally in doses of 0.1 cc. The usual site of injection is the inner surface of the forearm; no control test is considered necessary. The injected area should be observed in 24 to 36 hours. If a control is used, it should be realized that reactions to the control usually do not fade before 48 hours; therefore, comparison with the specific antigen should not be made within this period of time.

Applicable commercial name: Mumps Skin Test Antigen.

Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of mumps skin test antigen.

Mumps Vaccine.—A sterile suspension of mumps virus, grown in embryonated chicken eggs, inactivated by ultraviolet light or formaldehyde, and preserved with 1:10,000 thimerosal. Mumps vaccine is standardized for potency and antigenicity according to specifications of the National Institutes of Health.

Actions and Uses.—Mumps vaccine is used for active immunization against mumps. Detectable increases in antibody titer are apparent within one week after subcutaneous injection of the vaccine, but the duration of this actively acquired immunity is uncertain. Current evidence suggests that protection against the disease does not persist for longer than a year after vaccination. Thus, mumps vaccine does not confer the same degree of immunity as a naturally acquired infection. Although the vaccine may be given within two to three days after exposure, no information is at hand to indicate that the vaccine successfully aborts a clinical case of mumps or alters the course of the subsequent disease. Hence, vaccination is indicated only in certain restricted circumstances as a prophylactic measure before exposure. Since the clinical course of and sequelae to mumps are usually not severe in children and since a naturally acquired infection generally confers lifelong immunity, the use of the vaccine in children is justified only as a means of preventing widespread epidemics in those situations in which large numbers of children are kept in close proximity for long periods, as, for example, in orphanages or boarding schools. It is not advised for children in isolated circumstances. The vaccine may be employed prophylactically in adults when antibody titers or skin tests indicate a lack of immunity. If a vaccination is administered before exposure in such cases, the patient is less likely to develop clinical mumps and, hence, the potentially serious complications of orchitis and meningoencephalitis. As in the younger age group, vaccination of adults should generally be restricted to individuals who live in closely segregated populations where epidemic parotitis and its numerous sequelae may become a serious problem. Such groups are exemplified by military personnel, nurses, medical stu-

dents, and institutionalized or hospitalized patients. Fortifying or booster injections 6 to 12 months after primary immunization are desirable if protective antibody titers are to be maintained.

Since mumps vaccine is prepared from the embryonic fluid of chicken eggs, its administration is absolutely contraindicated to persons giving a history of hypersensitivity to egg, chicken, or chicken feathers. If there is a negative history of hypersensitivity and a pseudo-positive reaction indicating hypersensitivity develops from a skin test, subsequent use of mumps vaccine is contraindicated.

Dosage.—Mumps vaccine is administered subcutaneously. The immunizing dose for children and adults consists of two injections of 1 cc. each. The optimal interval between injections is not known, but periods of one to four weeks are usual. A booster dose of 1 cc. may be indicated after 6 to 12 months.

Applicable commercial name: Mumps Vaccine.

Lederle Laboratories Division, American Cyanamid Company; and Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of mumps vaccine.

Use of Isoflurophate in Strabismus

The Council previously has described the ophthalmic use of a 0.1% solution in peanut oil of the potent irreversible cholinesterase antagonist isoflurophate (Floropryl) in the treatment of certain forms of glaucoma. The Council has evaluated additional evidence for its ophthalmic use as a 0.025% ointment in the treatment of glaucoma as well as in the management of accommodative (nonparalytic) convergent strabismus (esotropia). The use of either concentration of the drug in glaucoma is based upon its miotic action, whereas the use of only the lower concentration in nonparalytic esotropia is based upon its peripheral stimulatory action on the intraocular muscles of accommodation. The latter action, if pronounced, may provoke disabling ciliary spasm accompanied by unpleasant side-effects, which may interfere with the use of the drug. Such effects usually tend to diminish or disappear with continued therapy. The potent miotic effect of the drug, even with the use of the lower concentration in the treatment of nonparalytic esotropia, has been associated with the development of iris cysts, which may obscure vision. Iris cystic involvement usually is reversible after withdrawal of the drug and often can be obviated by administration of dosage at infrequent intervals. However, if the drug is not effective for maintenance therapy when instilled at dosage intervals of 48 hours or longer, its use is contraindicated. Iris cysts appear in a large proportion of children after some weeks or months of administration of the drug at shorter intervals. In such instances the drug should be abandoned in favor of other forms of therapy.

From available evidence the Council concluded that ophthalmic use of the 0.025% ointment is suitable in strabismus when visual acuity is approximately equal in both eyes (1) as a diagnostic agent to estimate the factor of accommodative effort commonly encountered in hypermetropic nonparalytic esotropia, and (2) as a therapeutic agent to reduce or overcome the excessive centrally stimulated accommodative effort by substitution of peripherally stimulated accommodation in such cases. The Council also found some evidence to indicate that, when esotropia is complicated by anisometropia or amblyopia, the 0.025% concentration may be used only in the more affected eye. In amblyopic esotropia, in which use of the drug in the more affected eye is combined with use of atropine in the fixating eye, care is necessary to deatropinize the latter as soon as the former is fixating, to avoid amblyopia in the originally fixating eye. The drug also is used after corrective surgery to overcome residual esotropia due to excessive accommodative effort. Orthoptic training is considered desirable before initiating corrective drug therapy because such training is difficult in the presence of drug-induced miosis. Drug therapy may supplant or supplement the use of glasses in patients with little or no astigmatism, particularly in very young children, in childhood where social activities or behavior problems interfere with their use, and in the transition from use of glasses to their abandonment.

The Council reaffirmed the view that the drug is suitable only for ophthalmic use by conjunctival instillation, owing to its potentially profound systemic cholinergic effects; it may even be absorbed from accidental contact with the skin. Precautions are essential to avoid such contact, to wash away any of the drug accidentally spilled on the skin, and to prevent accidental ingestion by children or inadvertent injection of the drug into the tissues. Ophthalmic use is seldom if ever associated with systemic effects when the drug is used in the available concentrations according to the suggested dosage. Because the drug is rapidly hydrolyzed by water, care should be exercised to avoid washing the eye dropper with water or allowing it to come in contact with the conjunctival sac. The usual effective dosage of the 0.025% ointment in glaucoma is 1 drop (¼-in. extrusion from an opthalmic tube container) in the affected eye every 8 to 72 hours. Bedtime administration is desirable, if feasible, to minimize blurring of vision. In the initial estimation and management of nonparalytic esotropia, the usual dose is not more than 1 drop or ¼ in. of the ointment in each eye daily at bedtime for two weeks. If the drug proves beneficial, the dosage interval should be lengthened to 48 hours and up to as little as once weekly, depending on the least amount required to maintain binocular fixation without abnormal convergence.

The Council voted to revise New and Nonofficial Drugs to describe the use of isoflurophate in the management of nonparalytic esotropia.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of this additional use of isoflurophate.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

Edited Under the Direction of the Board of Trustees

Editor and Managing Publisher . . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Assistant Editors . . . . . WAYNE G. BRANDSTADT, M.D.
FREDERIC T. JUNG, M.D.
EDWARD R. PINCKNEY, M.D.
Assistant to the Editor . . . . . MILTON GOLIN
Editor for Medical Literature Abstracts . . GEORGE HALPERIN, M.D.
News Editor . . . . . CHARLES CHAPMAN

Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

THE NEW YORK MEETING

The largest meeting of the American Medical Association has been held, with New York City as the site and the physicians of New York state as the hosts. Doctors from over the world participated in a gathering that broke all previous attendance records. Between sessions at various hotels and at the Coliseum, visiting members of the medical profession experienced a week of meetings spiced with social activities that long will be remembered. Exhibitors, and others, may have complained of the costs they had to bear, as New York is not an inexpensive place for a meeting, but they at least enjoyed comfort at the new Coliseum. And with more more than 2,000 physicians serving as lecturers and demonstrators, with approximately 350 scientific exhibits and about an equal number of technical exhibits, comfort was important.

Prior to the opening of the meeting, sessions were held by the Board of Trustees, the Council on Medical Education and Hospitals, the Council on Medical Service, the Council on National Defense, the Conference of Presidents and Officers of State Medical Associations, and other groups. Watching these conferences in action would give anyone a broad appreciation of what makes up organized medicine today. And when it is realized that such meetings are held almost weekly in many parts of the country, it is possible to understand the modern demands placed on those responsible for medical care.

Since doctors are purveyors of health measures, it seems reasonable they should sample what they urge on others. At the New York meeting they could do this, and many had electrocardiograms, chest roentgenograms, and eye examinations. In 1955 and 1956 at A. M. A. meetings about 15% of examinations revealed some abnormality. For information to meet their needs as they examine patients, physicians could attend 46 medical motion pictures, diabetes conferences, pathology demonstrations, demonstrations on infants; in fact, they could attend lectures or demonstrations on subjects ranging from allergy to urology. Also heavily attended were the color television programs, the international film show—the first of its kind—and another "first"—a trans-Atlantic telephone arrangement between physicians and surgeons in England and physicians and surgeons in New York.

Elsewhere in this issue of THE JOURNAL (page 885) is a brief summary of some of the highlights of the annual session. A more complete report of the proceedings of the House of Delegates will appear in THE JOURNAL in several parts in the near future, as soon as the report is transcribed and made suitable for publication. In the meantime, special actions taken by the House of Delegates and its standing committees and the Board of Trustees and its standing committees will be reported in THE JOURNAL and in bulletins from the office of the Secretary of the Association.

HOW TO MEET AN EMERGENCY

Physicians, nurses, and medical students in one Texas community have proved that even the best of emergency equipment and supplies are not enough, in themselves, to provide adequate civil defense. To help illustrate this fact, they managed to assemble one of two 200-bed emergency hospitals in only 55 minutes, claiming a new speed record (see this issue, page 889). But the feat took a lot of preplanning, including nearly four days to lay out the contents of all 256 separate cartons of supplies and equipment furnished by the Federal Civil Defense Administration, then repacking and re-storing everything in a trailer for quick assembly. It also took imagination and teamwork, the kind that counts when a major disaster strikes. In a few days, monitors of this first national exercise involving emergency hospital units are slated to report their experience in the hope that some 2,000 other communities banking on FCDA hospital packages may grasp the importance of rehearsal for swift medical organization when the sudden need arises. Failure to realize this concept amounts to a false sense of security. Unless there is proper preparation through field trial, according to doctors who helped direct the exercise in Texas, it could take as long as seven days to set up an emergency hospital system. Seven days might well spell the difference between life and death to thousands of injured persons.

DR. GUNNAR GUNDERSEN—PRESIDENT-ELECT

In New York at the 106th Annual Meeting of the American Medical Association the House of Delegates elected Dr. Gunnar Gundersen, a surgeon from La Crosse, Wis., to be President-elect. Dr. Gundersen was born in La Crosse on April 6, 1897, attended high school in Oslo, Norway, and returned to the United States to attend the University of Wisconsin, where he got his B. S. degree in 1917. He obtained his M. D. degree at Columbia University in 1920 and returned to his home town to intern at the La Crosse Lutheran Hospital 1920-1922. He then entered practice with his father. In 1927 with three of his five physician brothers he founded the Gundersen Clinic in La Crosse. He has always been active in the organizational side of medicine. From 1931 to 1937 he was a member of the board of regents of the University of Wisconsin. In 1937 he was certified as a diplomate of the American Board of Surgery and in the same year became a member of the House of Delegates of the American Medical Association. He was president of the Wisconsin State Medical Society 1940-1941 and in 1942 became a member of the board of directors of

the La Crosse Trust Company. He served as member and president of the Wisconsin State Board of Health in the years 1943-1952.

In 1945 he and his brothers established the Adolf Gundersen Medical Foundation in memory of their father. This nonprofit organization grants fellowships to young physicians for advanced study in specialized fields, provides facilities and modern equipment for such studies, conducts investigations into the many unsolved problems of medicine and surgery, and provides free diagnostic services to indigent persons with complex medical problems. Dr. Gundersen has been a member of the Board of Trustees of the American Medical Association since 1948 and its chairman since 1955. When in 1951 the Joint Commission on Accreditation of Hospitals was formed, he became its first chairman and served in that capacity for two years. He is a fellow of the American College of Surgeons and of the International College of Surgeons and a member of the council of the World Medical Association and of the American Public Health Association.

Although he has always had a lively interest in sports, he has given up active participation in most of them, but he still considers vegetable gardening an ideal hobby and takes a personal interest in reforestation projects.

Dr. and Mrs. Gundersen have three children and five grandchildren. The older son, Gunnar Adolf, a graduate of Harvard Medical School and a certified radiologist, is now associated with the Gundersen Clinic in La Crosse. The younger son, Cameron B., was graduated from Boston University Medical School in 1956 and is interning in San Francisco. Their daughter Mary lives with her lawyer husband in Oslo, Norway.

GUNNAR GUNDERSEN, M.D.
PRESIDENT-ELECT OF THE AMERICAN MEDICAL ASSOCIATION

Dr. Gundersen is familiar with the broad problems of medical care. He has served on many committees representing the American Medical Association and has gained the respect and affection of all those with whom he has been associated. His medical background, his interests, and his natural ability will assure members of the American Medical Association of a successful, able, and understanding President when he assumes this office in 1958.

WEIGHT GAIN AND PREGNANCY

It has been common practice for physicians to set a limit on the weight their patients gain during pregnancy. The reasons usually given are that this (1) helps to prevent toxemia and long difficult labor and (2) adds to the patient's comfort and improves her appearance. No one is likely to deny the second of these reasons, but, because few valid statistical studies have been made to support the first, Thomson and Billewicz[1] in England and Brantley[2] in the United States have made such studies. The limit usually set is a gain of between 18 and 20 lb. (8 to 9 kg.) for the entire period of gestation. Many physicians, however, arrive at the ideal weight at term by adding 20 lb. to the ideal weight for the patient's age and height rather than the patient's usual weight before she became pregnant.

In the British study the weight gain of 4,214 married primiparas was observed. The patients were not admonished to control their weight. After delivery it was found that preeclamptic toxemia developed in only 2.6% of those whose average weekly weight gain between the 20th and 36th weeks of gestation did not exceed 0.5 lb. (0.2 kg.), whereas 26% of those who gained 1.75 lb. (0.8 kg.) or more showed signs of preeclampsia. Those gaining more than 1.5 lb. (0.7 kg.) a week between the 20th and 29th weeks had a relatively high expectation of preeclampsia unless the rate of weight gain fell below 1 lb. (0.5 kg.) a week between the 30th and 36th weeks. Brantley observed 368 pregnancies in 322 patients whose gestation progressed to or beyond the 36th week. The patient's ideal weight plus 18 lb. was aimed at, especially in those who were obese or hypertensive, but efforts at weight control were through gentle persuasion rather than dire threats of ruined health or serious complications. Dietary advice was given rather than specific dietary formulas. Amphetamine was given to some of the patients whose weight was hardest to control. In this series the usual weight before pregnancy did not influence weight gain. The average weight gain was 22.5 lb. (10 kg.), but about 38% gained 25 lb. (11 kg.) or more. Moderate toxemia occurred in two patients who gained about 34 lb. (15 kg.). Both of them showed a sharply increased rate of weight gain in the last six weeks of gestation.

Thomson and Billewicz found that the incidence of prematurity decreased as the average weekly weight gain increased, except that it rose when toward the end of pregnancy there was a marked gain in weight associated with preeclampsia. They concluded that the higher rate of premature deliveries in those with a low weight gain was probably the result of poor

1. Thomson, A. M., and Billewicz, W. Z.: Clinical Significance of Weight Trends During Pregnancy, Brit. M. J. **1**:243-247 (Feb. 2) 1957.

2. Brantley, J. T.: Significance of Weight Control in Pregnancy, North Carolina M. J. **18**:1-5 (Jan.) 1957.

fetal development. The perinatal infant death rate was least in those whose average weekly weight gain was moderate (0.8 to 1.5 lb.), as they escaped the hazards of toxemia associated with high weekly weight gains and prematurity associated with extremes of weight gain. In general, perinatal deaths were more closely related to prematurity than to toxemia. In Brantley's series labor was prolonged over 24 hours in three patients whose total weight gain was 20, 33, and 41 lb. (9, 15, and 19 kg.) respectively. Delivery was difficult in five patients whose weight gain ranged from 17 to 27 lb. (8 to 12 kg.) (average 22 lb. [10 kg.]).

Thomson and Billewicz concluded that a gain of more than 1 lb. a week after the fifth month of gestation calls for close observation of the patient for signs of toxemia, and that restriction of weight gain appears to reduce the incidence of eclampsia but not of preeclampsia. It has often been suggested that a sudden acceleration of the rate of weight gain is more significant than a high average gain, but this is not a reliable sign. Although the average weight gain is higher in patients with than in those without preeclampsia, and although the incidence of preeclampsia rises at the rate of weight gain increases, these facts may be of little prognostic value in individual cases. The only safe procedure is to observe each prospective mother at regular intervals, checking weight, urine, blood pressure, and general health throughout pregnancy. Rigorous attempts to control weight without good reason during pregnancy probably are not justified and in some instances may be harmful. The best argument for weight control, except when a medical problem is involved, is that it makes the patient more comfortable and improves her looks.

TOM D. SPIES, M.D.
AWARDED DISTINGUISHED SERVICE MEDAL

DR. SPIES RECEIVES DISTINGUISHED SERVICE MEDAL

One of the highest honors that can be awarded to a physician in this country, the gold Distinguished Service medal and citation of the American Medical Association, was presented to Dr. Tom D. Spies by the American Medical Association's President, Dr. David B. Allman, at the Inaugural Meeting in the Waldorf-Astoria Hotel on June 4 during the 106th Annual Meeting in New York. Dr. Spies was selected by the House of Delegates of the American Medical Association for outstanding work in the field of nutrition. Through his researches, pellagra in the southern United States and tropical sprue in Cuba and Puerto Rico have been virtually eliminated. Perhaps his greatest contribution has been his study of the dietary requirements for the preservation of tissue integrity whereby premature aging can be prevented.

Dr. Spies was born in Ravenna, Texas, September 21, 1902. He received his A.B. degree from the University of Texas in 1923 and his M.D. degree from Harvard University in 1927; interned at the Peter Bent Brigham Hospital in Boston 1928-1929; assisted Dr. F. B. Mallory in the Boston City Hospital 1929-1930, and interned at the Lakeview Hospital in Cleveland 1930-1931. Since his internships he has continuously held teaching and research positions. He was a teaching fellow and instructor at Western Reserve University 1931-1935 and was assistant and associate professor of medicine at the University of Cincinnati College of Medicine, where he was also director of investigation, department of internal medicine, 1935-1946. In 1947 he became a professor in the nutrition and metabolism and chemical department of Northwestern University Medical School, a position he still holds.

Dr. Spies has always found time for additional tasks bearing on his chief interests. In 1936 he became director of the nutrition clinic of the Hillman Hospital, Birmingham, Ala., and he has made this his permanent headquarters. Since 1950 this clinic has been a part of Northwestern University. Since 1943 Dr. Spies has been a member of the food and nutrition board of the National Research Council. From 1941 to 1947 he was a consultant to the Secretary of War on tropical medicine. He is co-author with R. R. Williams of the book "Vitamin B_1 and Its Use in Medicine," published in 1938. In the same year he was American delegate to the United International Congress of Tropical Medicine in Amsterdam and the following year to the third International Neurological Conference in Copenhagen.

Other honors have been given to Dr. Spies in the past. In 1939 he was given the John Phillips Memorial Award by the American College of Physicians and a citation by the Medical Association of Alabama; in 1941 he received the scientific award of the American Pharmaceutical Manufacturers Association; in 1943 he was awarded the Southern Medical Association's research medal; and in 1944 he received an honorary Sc.D. degree from the University of the South in Sewanee, Tenn. Dr. Spies is a certified diplomate of the American Board of Internal Medicine, a fellow of the American College of Physicians and the Royal Society of Tropical Medicine and Hygiene (England), and a member of numerous other professional societies. He is the 20th recipient of the Distinguished Service medal.

ORGANIZATION SECTION

ADDRESS OF PRESIDENT DWIGHT H. MURRAY BEFORE THE HOUSE OF DELEGATES

This morning I feel like a medical courier who has completed the appointed rounds in one swift year, and neither snow, nor rain, nor heat, nor gloom of night has kept him from his important task. Despite the elements, however, it has been a most perfect year for me. It has been a thrilling experience to have served in medicine's highest and most honored office, and it has been a proud distinction to have represented the world's greatest medical organization—the American Medical Association.

Any final report on my activities could stretch from here to Napa, Calif., but this morning I would like to squeeze that report into a short, compact, three-section package.

What Was Done

While it has been impossible to visit every state, I have tried to cover as many state medical meetings and as many county medical societies as possible. I also have attended many conferences of A. M. A. councils and departments.

It has been my pleasure to represent the A. M. A. before allied medical-health groups such as the American Hospital Association and the American Academy of General Practice, and before nonmedical organizations such as the American Bar Association, the National Association of Manufacturers, and the American Legion.

I was fortunate, too, to have the opportunity to spend the month of March, 1957, inspecting the armed forces' medical installations in the Pacific area. This trip was made possible by the A. M. A. and the surgeon general of the Navy. Finally, I have visited medical schools and talked with medical students from Georgia to Indiana to Texas to California to Formosa. At these schools my purpose was to discuss with the students the work of the A. M. A. and the benefits of membership.

What Was Stressed

During the year I have emphasized three vital subjects: the personal touch in medicine, the necessity for freedom in medical practice, and professional unity.

At the inaugural ceremony last year I urged that we find some way of combining modern scientific methods with the personal, friendly touch of the one-time family doctor. I am gratified with the results of this effort for more tender, loving care on the part of each physician for his patient. The restoration of the close personal relationship between all doctors and patients has not been accomplished as yet, but our profession is showing its desire to humanize and personalize the practice of modern medicine. The cold, brisk, and impersonal attitude toward patients is on its way out, and I say good riddance.

Six months ago, in Seattle, I called upon our profession to work for patient and professional freedom so that we all might continue to live in freedom. This message I have repeated across the land. I can say honestly that I never have had more personal satisfaction and more active medical support than I have had in bolstering freedom in the conduct of medical treatment and freedom in the choice of physician.

My thoughts on medical freedom are no different than they have ever been. For me, a little governmental control of the medical profession is too much control. A little always leads to more control. And control of one profession leads to control over another segment of American life, and so on until all groups are dominated by the government. Consequently, I have stressed this point: See to it that you as a physician keep medicine free so that it can continue to provide the best possible medical care.

Physicians in many states also have heard me proclaim that our profession needs to be united and informed at all times. Just as we use the teamwork approach in modern medical care, so we must use it in solving the socioeconomic issues before us. Working together we will act as a unit and speak with one voice, instead of many. And we will offer clarity of aims and objectives, instead of confusion of purpose.

While these three points—the personal touch, medical freedom, and medical unity—have been my principal themes, I also have talked—at length I am afraid—about accreditation, postgraduate education, and the positive story of the American Medical Association.

When speaking about accreditation, I have attempted to clarify the purposes of the Commission on the Accreditation of Hospitals and to point out how it is working with the profession and hospital administrators to establish the best possible care for patients. I have pointed out, too, the necessity of self-governing hospital staffs and the undesirability of hospitals entering into the practice of medicine.

"School-is-never-out-for-the-doctor" has been my message on several occasions. I have used this phase because an M.D. degree, along with internship or residency training, is only the beginning of medical education. Unlike 50 years ago, the modern physician faces the difficult problem of keeping abreast of developments in medical science. For him continuing education is essential if he is to give the best care to patients and advance the health of the community.

Finally, it has been my pleasant assignment to report the good story of the American Medical Association—its service to the profession and the public, its achievements in hundreds of medical areas, and its hopes for the betterment of public health. Here, too, I have stressed the importance of doctors belonging to the A. M. A. and bring a part of—and not a part from—the A. M. A.

Read before the 106th Annual Meeting of the American Medical Association, New York, June 3, 1957.

What Was Found

Many state medical societies are endeavering to improve and streamline their business operations and the entire management of their organizations. This, in my opinion, will help facilitate the management of their affairs and put them in a position to give even better service to their membership.

—There has been very little disagreement between the policies of the various state societies and those of the A. M. A., and there has been an earnest desire and effort on the part of state officers to cooperate in every way possible with the A. M. A.

—In some states there was a lack of attendance at the house of delegates sessions. However, such findings were not general.

—In almost every state, membership in the A. M. A. can be increased. My personal feeling is that too many younger physicians are still outside the A. M. A. Perhaps this is due to financial reasons or to a greater interest in a specialty group than the A. M. A. Whatever the reason, everyone should make a new effort to bring the younger physicians into the A. M. A., for membership will benefit them and their profession immensely.

—Most state scientific programs were practical and informative for the type of medical society member attending the sessions. However, in some areas physicians felt that programs covering a wider field of subjects would be more attractive and would improve attendance.

—In every state I visited there was a great interest and desire for postgraduate medical education. In those states where postgraduate courses have been expanded, or have been initiated, there has been wide and genuine acceptance. This has been true not only among specialists but also among general practitioners who are required to do postgraduate work for continued membership in their academy.

During my stewardship as President-elect and President, I made on-the-spot checks of the so-called doctor shortage because this subject has been before the public for many years and it often arises in press interviews.

My report to you is that there is no over-all doctor shortage. In a few areas there is maldistribution, and there is a shortage of physicians in general practice —in urban centers as well as in rural sections. And I might add that in a few areas there is an oversupply of those limiting their practice to a specialty.

Generally, however, doctor distribution is good and it is being improved through the work of the A. M. A. and state society physician placement services. A sufficient number of physicians also is being produced to handle the nation's health needs adequately. In recent years there has been a net increase of about 3,750 doctors annually, and this figure is sure to rise with increased medical school enrollment and the establishment of new four-year schools. Meanwhile, doctor efficiency continues to rise because of chemotherapy advances and the development of new techniques and instruments. In addition, doctors are living longer and practicing longer than ever.

I also found that in most states the federal Medicare program is operating successfully. Although there have been numerous complaints about the fee schedules and the cumbersome governmental forms, there is a sincere and earnest desire to make the program work as long as it remains the law of the land.

Now, before I turn in my suit, I would like to make a brief suggestion.

To every physician I offer the advice of a famous American general: "Never content yourself by doing your second best, however unimportant the occasion."

At no time should our profession do less than the great general advised. But I fear that in some instances our best has not been given. I base this conclusion on the numerous "voice-of-the-people" letters I have received during my term of office. Invariably, the letters of complaint have touched on three points: 1. Inability to get a doctor when wanted. 2. Lack of willingness on the part of doctors to answer night, week end, and holiday calls. 3. Overcharging in some instances.

If every physician were to give an extra measure of attention to these three areas, I am sure your incoming President, Dr. Allman, would have his volume of mail reduced by 75% or more.

Rather than making this just a suggestion, let me plead with you to take these matters to heart. Satisfied patients always have been, and always will be, our first line of defense against government domination of our profession. I know it is a difficult task to please every patient, but I ask you: Would it be easier to practice medicine as a servant of government?

Finally, allow me to testify as an expert witness on the state of affairs in the American Medical Association.

After 12 years as an A. M. A. officer and trustee, many years' experience as a delegate and chairman of the legislative committee, and 33 years in county and state medical society activities, I believe I am qualified to say that the A. M. A. is in a stronger and better position today than ever before. And I can think of at least three good reasons why it is—the headquarters staff, the Board of Trustees, and the House of Delegates.

Before I leave medicine's highest elective office, I want to thank personally the individual members of the headquarters' staff for their dedication and hard work. I only wish I had time to single out each man and woman, and give them the recognition they deserve.

Second, I want to pay a personal tribute to all the great men of medicine with whom I have served on the Board of Trustees during the past 12 years. Their efforts, their thoughts and ideas, and their good sound judgment—to say nothing of the hundreds of hours away from home—cannot be equaled by any group of men in the world. These self-sacrificing men serve our American Medical Association for the good of mankind and for the assistance they can give their colleagues in medicine.

All of these fine gentlemen of the Board of Trustees of the last 12 years are living, with the exception of Charles W. Roberts of Atlanta, Ga., Elmer L. Henderson of Louisville, Ky., and Thomas P. Murdock of Meriden, Conn. So, to all the past and present members of the Board, I salute you for your never-ending contributions to the betterment of medicine and the A. M. A.

Lastly, I extend my personal thanks to the House of Delegates and to every member for his untiring devotion. Since 1942 when I became a member of this

House, I have seen very few mistakes made by this great legislative group, and I wish to compliment you for your wisdom and foresight. I have every confidence that you will chart a wise course for our profession and for our Association.

I make only two appeals to you: Continue to adopt positive programs of action and service for the public, and be prepared to make even greater, far-reaching decisions in the future. As you know, medical problems never cease, and there are always new challenges to our profession.

In taking leave of this most highly respected office, the Presidency of the American Medical Association, I recall for you the fine words of that famous physician, Sir William Osler: "To have striven, to have made an effort, to have been true to certain ideals—this alone is worth the struggle."

ADDRESS OF PRESIDENT-ELECT DAVID B. ALLMAN BEFORE HOUSE OF DELEGATES

Our illustrious President has reported to you on his stewardship of office. He has served you well, with dignity and that rare quality of statesmanship so important to the preservation of the private practice of medicine. I heartily endorse the recommendations Dr. Murray has made. It is my fervent prayer that I may carry on as successfully during the coming year as he has during the past.

As is customary, I shall limit my remarks to a projection of what lies ahead rather than reporting to you on my year of internship as your President-elect. Although it has been arduous, it has made me more humble and proud of the honor you bestowed upon me in Chicago last year.

What course are we to chart for the coming year? What are the problems facing us? How may we advance toward that perennial objective of improved medical care for all of the American people? These are the questions we seek to answer each year as each succeeding President takes office.

There is no doubt in my mind that we are advancing toward that illusive goal which will always "exceed our grasp." But I am concerned whether our rate of progress is sufficient to keep pace with the rapid changes taking place in medical practice. In our struggle to advance socially as we have medically, have we made concessions which have tended to turn us away from our charted course? I would be less than frank if I did not express my concern.

I have encountered in recent months a feeling that the American Medical Association should "board the gravy train" of federal research appropriations. The argument is given that everyone is getting his share, so why should not the A. M. A. request financial support to conduct much-needed surveys in the medical care and socioeconomic fields. I have only two comments to make on this matter. If such surveys will help us to improve the quality and quantity of medical care being made available to the American people, then private capital or the American Medical Association itself should finance such studies.

Read before the 106th Annual Meeting of the American Medical Association, New York, June 3, 1957.

Furthermore, I am convinced that our Association's general position in support of economy in the federal government will be substantially weakened if we, too, line up at the "public trough." I hope that you feel the same way.

Federal legislation, after it has become the law of the land, has at times detoured us into dangerous areas. I have in mind here the request by certain hospitals for payments from the Department of Defense under Medicare for professional services rendered to dependents of servicemen by hospital residents. We should not lose sight of the fact that our residency training programs are teaching programs, and the sale of physicians' services by hospitals should be resisted. Furthermore, it is not in keeping with traditional patterns of medical practice and would encourage charges by hospitals for residents' services to patients not under the Medicare program.

Since I am on this subject, I should like to make one general comment on all third-party contractual agreements which call for fixed fee schedules. My concern in this area is not related to physicians' incomes but to the fundamental dangers inherent in standardized fees. Expediency, laws, and governmental regulations have encouraged us to accept fixed fees for specified groups, especially those in certain income brackets. We now find many prepayment plans raising their income ceilings to include a majority of our population. In my opinion, the pressure for this action is related primarily to competitive factors. Where will this trend lead? It has the inherent danger of ultimately affecting the quality of care rendered and should be carefully watched.

Traditionally, medicine has operated in a competitive climate that fosters incentive, rewards ability, and smothers mediocrity. But, as we all know, medicine has had to yield in the face of government intervention, although every effort has been made to retain its basic tenets. Medicine has yielded to financing mechanisms that clearly and without question restrict the seller's right to seek a reasonable price for his services—but only when it was convinced that the only alternative was submission to even less acceptable conditions.

Need for Constant Vigilance

If we really believe in our contention that a leveling or averaging process inevitably tends to destroy individuality and initiative, then there is cause for concern and a need for constant vigilance on the part of every physician.

Clarence Randall, in his book "The American Way," makes this observation: "The outward manifestation of the American system at work is freedom of choice for the individual in every activity of his life and the means of satisfying his own needs as he conceives them to be needs, the more willingly will he give of his best efforts in order that those ends may be attained."

In the area of voluntary health insurance, the American Medical Association from the beginning has consistently supported the service and indemnity approach as means of assisting the general public in financing health care. This diversification has resulted in the opportunity to test and adopt or reject many different prepayment concepts.

There are promising experiments in progress. The Wisconsin Blue Shield Plan, which combines a service concept with no fee schedule or income ceiling, deserves serious attention. The rapid growth of the so-called major hospital and medical expense coverage plans is encouraging. For the insured it provides a much greater bulwark of protection, while at the same time it has built in controls against abuse.

To those physicians who are board members of medical society–sponsored plans, I would encourage a thorough appraisal of the present status of your prepayment program. You should also give serious consideration to expanding your services to include deductible and co-insurance provisions. I believe there are a number of Blue Shield Plans now experimenting with this type of coverage.

In the realm of public service, the profession is to be complimented on the outstanding cooperation exhibited in the recent poliomyelitis vaccination campaign. Under the leadership of the A. M. A., state and county medical society poliomyelitis vaccination programs mushroomed to unprecedented proportions across the nation.

Unfortunately, the supply of vaccine made it necessary to curtail many well-planned programs. With production stepped up and anticipated supply now meeting demands, I would like to encourage your continued interest and participation in this public service campaign during the coming year.

Time does not permit the discussion of other problem areas and public service opportunities. It is apparent that the coming year presents many challenges which demand the cooperation of every practicing physician in America.

If we are to carry forward the spirit, the intent, and the promise of ever-improved medical care, we must be ready to bear the fatigues of supporting it. To this end, I pledge my time and talents during the coming year as your President.

THE THIRD PARTY IN MEDICINE

Congressman Oren Harris

I consider it a great honor that you have asked me to address you today. I may assume, of course, that you do not expect me to impart to you any knowledge in the field of medicine, which I do not possess. I would rather think that you want me to discuss some issues which concern both physicians and members of Congress, because legislative proposals involving these issues have been entertained in the Congress in the past and are apt to be considered again in the future.

Role of Interstate and Foreign Commerce Committee

Not a day passes on which I as an individual member of Congress or as chairman of the Interstate and Foreign Commerce Committee do not receive a number of communications involving some questions of health and health care. You may wonder why the Committee on Interstate and Foreign Commerce of all congressional committees should concern itself with questions of health. Certainly the name of the committee does not appear to imply any such concern. As frequently is the case, the explanation is a historical one and readily explains the connection between commerce and health.

Since colonial days our country has depended on merchant vessels to bring goods from foreign lands to our shores and to carry our exports abroad. Merchant seamen manning these vessels, when falling ill or becoming incapacitated, imposed an undue burden upon local facilities and local resources in our port cities.

When the Congress met in 1789, a resolution was adopted appointing a committee to prepare a bill providing for the establishment of hospitals for sick and disabled seamen. However, no such legislation was enacted until nine years later, when the 5th Congress passed an act to establish the Marine Hospital Service (I might say parenthetically that things today are still pretty much the same as they were during the early days of the Republic—it usually takes several sessions of Congress to develop and pass major legislation).

The Marine Hospital Service Act was approved by President Adams on July 16, 1798. It authorized the President ". . . to nominate and appoint, in such ports of the United States as he may think proper, one or more persons, to be called directors of the marine hospital of the United States, whose duty it is . . . to provide for the accomodation of sick and disabled seamen . . ."

The Marine Hospital Service formed the basis of the United States Public Health Service as we know it today, and from this interesting bit of history you will appreciate the historical connection between commerce and health which has resulted in the assignment to the Committee on Interstate and Foreign Commerce of legislative jurisdiction over public health and health care problems.

I would like to make it abundantly clear that the Committee on Interstate and Foreign Commerce feels very strongly that its responsibility in the field of health is one of the most important legislative responsibilities given to it, and the committee takes these responsibilities very seriously indeed. This field of the committee's legislative responsibility differs somewhat from other fields assigned to it, because in the case of health legislation the committee deals with human needs of all of our citizens. In many of the other legislative fields assigned to us we are dealing primarily with business organizations and trade associations, etc., and economic considerations frequently predominate, and necessarily so.

In an effort to more effectively discharge the committee's responsibilities in the field of health, I have as chairman of the committee appointed a subcommittee on health and science, of 11 members, with Congressman John Bell Williams of Mississippi as chairman. It is my purpose to see that special attention is given to the problems and legislation in these two fields. It is also my aim that this subcommittee of able members of the Congress keep in mind in the consideration of these matters, the subject which I have in mind for you today—"The Third Party in Medicine."

Chairman, Interstate and Foreign Commerce Committee, House of Representatives.

Read before the Conference of Presidents and Other Officers of State Medical Associations, New York, June 2, 1957.

I have not related to you the history of our committee's legislative responsibilities in the field of health, but merely explained why our committee and not some other congressional committee has legislative jurisdiction over health measures. I wanted, however, to call to your attention that from the very inception of the Republic, Congress, in case it found such action was justified on the basis of a clearly established need, has accepted the fact that a "third party" might be required in special situations to provide needed medical services.

Nature and Purpose of "Third Parties"

Every thoughtful person appreciates, no doubt, that a "third party" entering into a two-party relationship creates quite a problem. In the case of a marriage relationship, intervention of a "third party" almost invariably results in a breaking up of the marriage. Fortunately, however, this is not the rule with regard to all "third parties." Take, for example, the case of the relationship between a member of Congress and his constituents. A "third party," in the form of an interested group or an executive agency, might attempt to influence the congressman-constituent relationship. Quite frequently a "third party" may improve this relationship by helping both the constituent and the congressman. Then, there are other instances where nothing is further from the mind of a "third party" than to strengthen the relationship between the congressman and his constituent, but, on the contrary, this party is out to sever the relationship and to sever it for good.

What am I trying to say? I am trying to say that in the case of the relationship between a physician and his patients, just as in the case of other relationships, each case of a "third party" must be examined carefully on its own merits in order to determine whether the "third party" is likely to benefit or harm the relationship.

Let me examine then the nature and purpose of some of the "third parties" which participate in the physician-patient relationship and let us try to determine whether their participation has been beneficial or adverse. I do not mean with a view of determining the advisability of whether they are good or bad. Most of us have our own opinions about some of these programs. I merely wish to point to some results and with particular emphasis to the trend of today.

Hospitals as "Third Parties"

Let us take hospitals, for example. Surely they must be considered "third parties" when it comes to the doctor-patient relationship. However, could you imagine practicing medicine today without hospitals? As a matter of fact, it might be said that the construction of many hospitals, particularly in rural areas and small communities, has contributed to the establishment of new physician-patient relationships, because in many instances physicians could be induced to practice medicine in rural areas and small communities only after adequate hospital facilities were made available in those areas. Hospitals also help train new members of your profession by providing the facilities where medical students, interns, and residents gain the practical experience required by physicians.

If we consider hospitals "third parties," then can we consider the federal government a "third party—once removed" because the federal government, through the hospital construction program, has given impetus and support to the construction of new hospital facilities by state and local governments and private, nonprofit organizations?

While hospitals on the whole must be considered "third parties" which greatly benefit the physician-patient relationship, there have been some instances in which some hospitals have been criticized for disturbing established physician-patient relationships. Such criticism has come from physicians as well as from patients. It has been directed against the practice generally followed by hospitals of being selective about admitting members of the medical profession to their staffs. This selectivity (and I am not criticizing it when I refer to it) definitely affects the relationship between some physicians and some patients.

Where does that leave the hospitals as "third parties"? On balance, I would think, your profession would not want to do without hospitals. This does not mean however that each and every act of these "third parties" invariably is beneficial to the relationship which exists between a given physician and his patients.

Other "Third Parties"

Let us look at some other "third parties." Their number has become legion in recent years. Private insurance carriers and prepayment organizations have increasingly become "third parties" which importantly participate in the physician-patient relationship. These carriers may be commercial insurance companies, or they may be nonprofit organizations like the Blue Cross or Blue Shield. They may be prepayment plans organized by employers or employees, or they may be organized jointly by both employers and employees. They may be prepayment plans organized by consumers on a communitywide basis, or they may be prepayment plans organized by local medical societies which compete with consumer-sponsored prepayment plans.

All of these "third parties" greatly differ from each other with regard to the method which they employ in participating in the physician-patient relationship. Your profession, through its local, state, and national organizations, has scrutinized, and appropriately so, these methods for many years. You have approved some and you have actively opposed others. As I understand it there are many different points of view as to whether a given plan or method is beneficial or detrimental to the traditional physician-patient relationship.

This is a fundamental issue that has beset many members of Congress, and especially the members of our committee, in the consideration of the many proposals and, I might say, demands which we have had in matters of public health. I am personally concerned about the trend in the thinking that goes into these legislative proposals but want to emphasize here that this is the fundamental principle involved between the traditional system, the freedom and unrestrained relationship on the one hand, and governmental interference, or often referred to as socialized medicine, on the other.

As new "third parties" appear on the scene, new issues will be raised for some time to come and perhaps the debate will become heated in particular cases to the point where some of these controversies will, as they have in the past, reach the courts, state legislatures, and the Congress of the United States.

There are other "third parties" that are not thought of quite as frequently as "third parties" because their attempts to influence the traditional physician-patient relationship are of a different character. I have in mind drug and pharmaceutical firms on the one hand and foundations and voluntary associations operating in the health field on the other hand.

The Committee has received a number of interesting communications from members of your profession pointing to the increasing amount of advertising engaged in by some pharmaceutical firms addressed to the public in general. The purpose of this advertising obviously is to create a demand on the part of the general public for particular drugs. Some of these drugs may be sold on prescription only. Therefore, such public advertising is aimed at creating a demand on the part of the patients that physicians prescribe particular drugs. Thus, the pharmaceutical houses engaged in such advertising seek to influence the physician-patient relationship. Some physicians who have communicated with our committee have suggested that such advertising constitutes an unwarranted interference on the part of the particular drug manufacturer in the traditional physician-patient relationship. It is my understanding that the problems have been the subject of study by a special committee established by the American Medical Association. If these practices continue and increase in frequency, our committee too may desire to study how these practices affect the public welfare, or should I say public "tranquility."

Public demand for particular drugs, or biological products, is created not only on the basis of public advertisements. Foundations and voluntary organizations concerned with particular diseases aim at reaching the public to arouse interest in these specific diseases and to stimulate their prevention or cure. In some instances substantial differences of opinion have arisen on the part of medical experts on whether a vaccine or a pharmaceutical or biological product is safe and efficacious and whether it should or should not be given to patients. There might be further disagreement among medical experts with regard to the methods which should be employed in applying the vaccine or the pharmaceutical product. The direct contact, however, which a foundation or other organization may have with the general public may greatly influence traditional physician-patient relationships. We cannot easily forget an experience so recently which pointed so forcefully to this particular problem.

The Government as a "Third Party"

So, you can see we have a multitude of "third parties" which seek to participate in the physician-patient relationship. Some of the "third parties" have become generally accepted by physicians and patients. As to other "third parties" the situation is often not so clear, and this is particularly true with regard to some of the more recent "third parties" whose potential power for good or evil is very great indeed. As an example, you have the existing contentions which have arisen recently on certain kinds of prepayment plans.

It is impossible for me to discuss the benefits and disadvantages, both actual and substantial, of all of the "third parties" that I have referred to so far. Therefore, I would like to single out for attention one "third party" to whose role with regard to the traditional physician-patient relationship I have given particular thought—and I refer to the federal government as a "third party in medicine."

How are we to judge the role of the federal government as a "third party"? In order to do this we must be ever mindful of the nature of the physician-patient relationship.

In spite of the general tendency toward increasing specialization on the part of the medical practitioner, modern medicine appears to stress more and more the interrelationship of all human functions and the need for dealing with the whole person of the patient. This concept of medicine requires more than ever a peculiar relationship of confidence between patient and physician. Any attempt to make this relationship of confidence over into a service which can be routinized or standardized and which may be purchased at a going price in the market place can only result in destroying that relationship. This does not mean, however, that ways and means might not be found in the future by the medical profession on the basis of carefully conducted experiments of facilitating the rendering of medical services through the utilization of new and improved methods of prevention, diagnosis, and treatment.

If this personal relationship of confidence is to be preserved—and I, for one, am determined that it will be—it follows that the role of the federal government as a "third party" in that relationship must be carefully circumscribed if it is to further and not harm that relationship.

We might postulate, first, that the federal government should not play any "third party" role unless there is a clearly demonstrated actual need for such a role, and unless there is substantial agreement that such need cannot be met in any other way.

Secondly, we might say that after the actual need has been clearly demonstrated, and after substantial agreement has been reached that the federal government should become a "third party," then the needs should be met, wherever possible, through indirect rather than direct methods. In other words, the federal role should not be, except in special circumstances like in the case of our armed forces, for example, to provide medical services but to help provide the facilities in which, or to create the conditions under which, physicians are enabled to furnish the needed medical services without further participation of the federal government.

I believe that these two yardsticks—the yardstick of clearly demonstrated actual need and the yardstick of indirectness—have been employed by the medical profession in judging the merits—or the lack thereof—of health legislation. Those legislative programs which the medical profession has supported in the past, such as programs for federal aid in the construction of hospitals and research facilities, have met this dual test of need and indirectness.

Another program which is pending before our committee, calling for federal aid for the construction of medical school facilities, likewise appears to meet these two tests and thus is receiving your support. Even though there is great urgency for this program to meet an emergency with the economy wave and the consciousness of ever great federal responsibilities I have as chairman of the committee experienced difficulty thus far in getting off of the ground with further authorization. Our committee has observed the caution sign emanating throughout the country.

The fact that in the case of some programs the federal government is an "indirect third party" does not mean at all that it is an "insignificant third party." Take the appropriations for the National Institutes of Health for medical research. These have grown over a 20-year period from slightly less than one-half million dollars in 1938 to more than 220 million dollars in 1958.

In the case of the Hill-Burton program, federal funds appropriated for the current fiscal year amount to 125 million dollars, and the budget request for the next fiscal year is only slightly less. Since the inception of the program in 1946, the Congress has appropriated over 937 million dollars for the construction of hospitals.

On the other hand, plans calling for compulsory health insurance which would have resulted in a substantial curtailment of the independent character of private insurance carriers and prepayment organizations have met with your spirited opposition, and I can truly say, mine too, consistently. I venture to say that in regard to that proposal you probably felt that there appeared to be no clearly demonstrated need for such a far-reaching program, and that the methods proposed in these measures directly injected the federal government as a "third party" in physician-patient relations.

Finally, let me say that in my judgment the Committee on Interstate and Foreign Commerce, whenever health legislation comes before it for consideration, will exercise the greatest care to see to it that the federal government does not unnecessarily become a "third party" in medicine. When a need for federal participation has clearly been established, the committee will examine the proposal to determine whether the methods by which the federal government would be called upon to participate are such that they will not adversely affect the all important relationship of confidence that must exist between physician and patient.

I want to remind you, however, that the American people have always felt free to call upon Congress to act in any area of their lives if they feel that a need for action exists. As you well know, a considerable amount of public attention has been focused on the high cost of medical care (of which doctors' fees are only a part). If the American people should feel that large segments of the population, as, for example, the aged or the chronically ill, are unable to secure adequate medical care because the cost of such medical care is beyond their ability to pay, then they will call upon the Congress to meet these needs.

In this respect the American people have changed little if any since the days when the famous Frenchman, Alexis de Tocqueville, visited these shores. Upon his return to France in 1830 he wrote: "These Americans are the most peculiar people in the world. You will not believe it when I tell you how they behave. In a local community in their country a citizen may conceive of some need which is not being met. What does he do? He goes across the street and discusses it with his neighbor. Then what happens? A committee comes into existence and then the committee begins functioning on behalf of that need."

Today, when individual needs remain unmet, through the efforts of private groups or through local or state government programs, the outcry to have something done in behalf of these needs reaches the Congress with increasing frequency.

I hope that some of the serious health needs to which I have referred can be met by your profession with the aid of private "third parties." If they are not met in this manner, public pressure will be growing steadily about enlarging the area in which the federal government should participate as a "third party in medicine." The dangers inherent in such expansion of the federal role in medicine are very real indeed, and much is at stake for your profession. I am confident, therefore, that you will not slacken in your effort to participate actively in trying to meet some of these urgent needs.

HIGHLIGHTS OF RECORD-SETTING NEW YORK MEETING

Following is a summary of highlights of the 106th Annual Meeting of the American Medical Association, with special emphasis on actions of the House of Delegates. Earlier issues of THE JOURNAL *carried some advance reports and resolutions as well as brief statements of officers. Future issues will carry an abstract of the proceedings, which eventually will be presented fully, in pamphlet form.*—ED.

Alert concern with health problems in a growingly complex society has been demonstrated by the American Medical Association's House of Delegates.

The session in New York City June 3 through 7 attracted a registration of some 19,600 physicians to clinical, organizational, and technical activities—making it the most heavily attended convention in the 110-year life of the A. M. A. Indeed, the registration marks this as history's largest assemblage of physicians in any city at one time. The previous record of 17,958 registrants was set four years ago, also in New York.

Showing increased concern with socioeconomic topics, organized medicine's 192-man parliament acted decisively on such matters as ethics, Medicare, social security, occupational health programs, and relationships between medical societies and union-sponsored medical projects.

In between considerations of 66 resolutions, the House of Delegates elected 16 men to official positions. Members unanimously chose Dr. Gunnar Gundersen, 60-year-old surgeon from La Crosse, Wis., as the A. M. A.'s President-elect for the coming year—elevating him from his previous post as chairman of the Board of Trustees. Later the trustees selected as their new chairman Dr. Edwin S. Hamilton, 67, of Kankakee, Ill.

Dr. Gundersen will become President of the A. M. A. at its 107th Annual Meeting in San Francisco next June, on expiration of the term of Dr. David B. Allman, the Atlantic City surgeon who was inducted into the top A. M. A. position June 4 at the New York meeting.

Organized medicine's highest honor of the year—the Distinguished Service award—was voted to Dr. Tom D. Spies, 55, for outstanding contributions to the science of human nutrition. Dr. Spies heads the department of nutrition and metabolism at Northwestern University Medical School in Chicago and is director of the nutrition clinic at Hillman Hospital in Birmingham, Ala.

For the third time in history the A. M. A. awarded a citation to a layman for distinguished service. The recipient is Henry Viscardi Jr., of West Hempstead, N. Y., 44, founder and president of Abilities, Inc., which employs only severely disabled persons. He himself was born without legs.

The House of Delegates also cited Parke, Davis & Company, Detroit pharmaceutical firm, for its continuing series of institutional messages in national magazines "which accurately and dramatically tell the story of medicine and medical progress." The Goldberger award, to honor physicians who have made important contributions to the knowledge of nutrition, was presented to Dr. Paul Gyorgy, professor of pediatrics at the Hospital of the University of Pennsylvania.

New members elected to the nine-man A. M. A. Board of Trustees are Drs. Cleon A. Nafe of Indianapolis and George M. Fister of Ogden, Utah, both of whose terms expire in 1962; Dr. James Z. Appel of Lancaster, Pa., who fills the unexpired term (ending in 1960) of the late Dr. Thomas P. Murdock; and Dr. Raymond M. McKeown of Coos Bay, Ore., finishing the remaining year of Dr. Gundersen's term.

Dr. Jesse D. Hamer of Phoenix, Ariz., was elected unanimously as Vice-president, and similar votes of acclamation reelected Drs. George F. Lull of Chicago as Secretary, J. J. Moore of Chicago as Treasurer, E. Vincent Askey of Los Angeles as Speaker of the House of Delegates, and Louis M. Orr of Orlando, Fla., as Vice-speaker.

The Scene

This month's Annual Meeting marks the seventh time that the A. M. A. has convened in New York City and the first time that its technical exposition was able to take advantage of facilities in the new Coliseum. There, physicians viewed over 500 technical and scientific exhibits, heard papers of more than 400 physicians, attended showings of medical films and live color telecasts, and took part in section meetings covering all branches of medicine.

Less than 2 miles away sat the House of Delegates in the grand ballroom of its headquarters hotel, the Waldorf Astoria. Allied medical meetings also took place there and in at least a dozen other New York hotels.

For the first time in history, groups of American and British physicians (June 5) were able to confer during meetings in their respective home countries—thanks to a telephone link via the new underseas cable connecting an American audience of doctors in Carnegie Hall and physicians at the Harvey Tercentenary Congress in London. The hookup was arranged by Smith, Kline & French Laboratories. This "one medical world" motif began a day earlier in the Barbizon Plaza Hotel, where a three and a half day international medical film exposition began.

While in the city, physicians—many of them with their families—managed to sandwich in rare moments of tourist pleasure. They stood at observatory towers, toured famous buildings and museums, visited New York's medical schools and hospitals, attended the theater and television shows, shopped along the avenues, and sampled food in the city's many fine eating places. They also golfed, swam, and watched major league baseball.

The entertainment highlight in New York was the President's reception and ball following Dr. Allman's inaugural ceremony; this was attended by a capacity throng and was televised for New York viewers by cameras on special platforms in the Grand Ballroom.

The Action

Following are some highlight actions of the House of Delegates:

Medical Ethics.—The House ratified, by unanimous vote, a revision of the A. M. A.'s proposed Principles of Medical Ethics as drafted in condensed form at the Clinical Session in Seattle last November—but with changes in sections 6, 7, and 10. The revision, as adopted, reads as follows:

Preamble

These principles are intended to aid physicians individually and collectively in maintaining a high level of ethical conduct. They are not laws but standards by which a physician may determine the propriety of his conduct in his relationship with patients, with colleagues, with members of allied professions, and with the public.

Section 1.—The principal objective of the medical profession is to render service to humanity with full respect for the dignity of man. Physicians should merit the confidence of patients entrusted to their care, rendering to each a full measure of service and devotion.

Section 2.—Physicians should strive continually to improve medical knowledge and skill, and should make available to their patients and colleagues the benefits of their professional attainments.

Section 3.—A physician should practice a method of healing founded on a scientific basis; and he should not voluntarily associate professionally with anyone who violates this principle.

Section 4.—The medical profession should safeguard the public and itself against physicians deficient in moral character or professional competence. Physicians should observe all laws, uphold the dignity and honor of the profession and accept its self-imposed disciplines. They should expose, without hesitation, illegal or unethical conduct of fellow members of the profession.

Section 5.—A physician may choose whom he will serve. In an emergency, however, he should render service to the best of his ability. Having undertaken the care of a patient, he may not neglect him; and unless he has been discharged he may discontinue his services only after giving adequate notice. He should not solicit patients.

Section 6.—A physician should not dispose of his services under terms or conditions which tend to interfere with or impair the free and complete exercise of his medical judgment and skill or tend to cause a deterioration of the quality of medical care.

Section 7.—In the practice of medicine a physician should limit the source of his professional income to medical services actually rendered by him, or under his supervision, to his patients. His fee should be commensurate with the services rendered and the patient's ability to pay. He should neither pay nor receive a com-

mission for referral of patients. Drugs, remedies or appliances may be dispensed or supplied by the physician provided it is in the best interests of the patient.

Section 8.—A physician should seek consultation upon request; in doubtful or difficult cases; or whenever it appears that the quality of medical service may be enhanced thereby.

Section 9.—A physician may not reveal the confidences entrusted to him in the course of medical attendance, or the deficiencies he may observe in the character of patients, unless he is required to do so by law or unless it becomes necessary in order to protect the welfare of the individual or of the community.

Section 10.—The honored ideals of the medical profession imply that the responsibilities of the physician extend not only to the individual, but also to society where these responsibilities deserve his interest and participation in activities which have the purpose of improving both the health and the well-being of the individual and the community.

In presenting its revised and amended version of the Principles, the reference committee cited "Guides for Conduct for Physicians in Relationships with Institutions," which was voted by the House of Delegates in 1951. The reference committee went on to state that the Guides "make it clear that the type of financial arrangement between a physician and a hospital, corporation or other lay body is important and *relevent* in determining whether or not such an arrangement is ethical. We further believe that the amount of a physician's income or whether or not an institution is making a profit on his services is *irrelevant* in determining whether an arrangement is ethical."

In another action on ethics, the House of Delegates voted approval of a resolution (sponsored by the New York delegation) which provided that "in those states which have their own Principles of Professional Conduct (or Ethics) those Principles shall be binding upon all the members of the state society or association providing they are not inconsistent or in conflict with the constitution and by-laws of the American Medical Association." New York state has a more specific code of ethics than does the A. M. A., and thus is in a position to enforce it as a result of the latest action.

Corporate Practice of Medicine.—In voting acceptance of a reference committee criticism of "the illegal corporate practice of medicine," the House of Delegates agreed with the following statement of the committee:

> Your reference committee is impressed by the necessity of informing all physicians and the general public as to the evils which may be inherent in the socialization of medicine through corporate activity as well as by government action. . . . In many of its forms it is indistinguishable in practice and effect from socialization of medicine and appears to embody all its evils. . . . Your reference committee therefore recommends that this problem be referred to the Board of Trustees with the request that it devise and initiate a campaign to educate both physicians and the general public as to the dangers inherent in the illegal corporate practice of medicine in its various forms.

Intervention of a Third Party on the Physician-Patient Relationship.—The House of Delegates voted to accept—with revisions—a report made to the Board of Trustees by a Joint A. M. A. Committee on Medical Care for Industrial Workers. This report cited issues involving local medical societies and the United Mine Workers Fund, and the Committee drew up "General Guides" governing responsibilities of both sides. While approving the report (to be published in a later issue of THE JOURNAL), the House of Delegates amended the "General Guides" so as to preserve not only free choice of physician but also free choice of hospital by the patient. Also added were the following two "fundamental concepts": 1. "A fee for service method of payment for physicians should be maintained except under unusual circumstances. These unusual circumstances shall be determined to exist only after a conference of the liaison committee and representatives of the fund." 2. "The qualifications of physicians to be on the hospital staff, and membership on hospital staffs is to be determined solely by local hospital staffs and local governing boards of hospitals."

Five resolutions dealing with free choice of physician had been placed before the House but none was adopted on the ground that their intent was covered by the adopted "General Guides."

Social Security.—Six resolutions relating to Social Security were sent to a reference committee for action. One, offered by the New York delegation and calling for extension of "the benefits of Social Security to self-employed doctors of Medicine," was defeated by a voice vote. A similar resolution, in which the Connecticut delegation called for compulsory inclusion of physicians under the Social Security law, was voted down the same way. Adopted were three other resolutions supporting participation of physicians in pension plans for the self-employed, such as that advocated in Congress in the Jenkins-Keogh bills.

The House of Delegates voted unanimously to:

> reaffirm its long-standing opposition to the compulsory coverage of physicians under the Old Age and Survivors Insurance provisions of the Social Security act. . . . The pattern of social insurance schemes in other countries growing from retirement payments to survivorship payments to permanent and total disability payments to temporary cash sickness benefits and, finally, to national compulsory health insurance, is all too clear. The Association's position favoring the Jenkins-Keogh bills is a more logical approach, as it encourages thrift and discourages inflation and dependence upon the federal government.

Dependent Medical Care (Medicare).—The House of Delegates restated suggestions made to the federal government before Medicare was instituted last December—suggestions which opposed setting of any fixed fee schedule. It noted that several states have negotiated contracts without a published fee schedule, and added, "We are recommending that the decision as to the type of contract and whether or not a fee schedule is included in future contract negotiations should be left to individual state determination, keeping in mind the . . . suggestions. The American Medical Association should request the Secretary of Defense to modify the program so it can be operated as an indemnity-type program."

Then the delegates adopted a resolution condemning Medicare payment "to or on behalf of any resident, fellow, intern or other house officer in similar status who is participating in a training program." Eight reasons were stated for this action.

Occupational Health Programs.—By unanimous vote the House of Delegates adopted a report setting down, for the first time, "Scope, Objectives, and Functions of Occupational Health Programs," making a half-dozen slight revisions in wording. "It marks the needs and boundaries of occupational medicine," the reference committee reported. "It states in a positive fashion the proper place of occupational health programs in

the practice of medicine and it clearly charts the pathways of communication between physicians in occupational health programs and physicians in the private practice of medicine." The pioneer document covers work environment, health examinations, records, diagnosis and treatment, and health and safety education.

Medical Education.—The House of Delegates voted unanimously to adopt "Functions and Structure of a Modern Medical School" (published in the Handbook and in THE JOURNAL, May 4, 1957, page 58) to replace "Essentials of an Acceptable Medical School." Reported the reference committee: "The very fact that the 'Functions' were arrived at in collaboration with the Association of American Medical Colleges indicates the close relationship between the American Medical Association and the medical educators of the United States."

Also adopted, with some amendment, were "Guides and Basic Principles of Postgraduate Medical Education" (published earlier in the Handbook and in the May 4 issue of THE JOURNAL, page 61). The House of Delegates inserted this paragraph in the "Guides": "Strictly as aids to education rather than as the sole method, the use of colored slides, motion pictures and color television is encouraged. In the case of home study courses, the use of television and other audiovisual kits may be included. However, the import of television to medical education is still in the exploratory and experimental phase."

"Medical education today is in a state of extreme experimentation aimed at improving the methods, requirement, time, etc.," according to the reference committee's accepted report.

> This includes the full gamut of the problem of premedical, undergraduate, graduate and postgraduate medical education. . . . Your reference committee is still convinced that a sound, well-organized rotating internship meets the present needs of medical education in a superior manner to the straight internship. The Council should continue the encouragement of rotating internships. It may recognize the straight internship only in situations of superior content and for the purpose of studying new methods of medical education.

Other House of Delegates Action

The House of Delegates also:

—Was "impressed" with the fact that the A. M. A.'s net worth in the past 11 years increased from some $7,000,000 to more than $11,300,000. "This increase in assets reflects sound management of the Association's fiscal affairs by the Board of Trustees, general officers and Secretary-General Manager. It is recognized that a substantial portion of this fiscal growth is directly attributable to successes enjoyed by THE JOURNAL."

—Recommended that the Committee on Rehabilitation explore the establishment of an integrated consultation service to guide local professional groups "in dealing with the total program of rehabilitation."

—"Concurs heartily with the Board [of Trustees] that the House of Delegates meeting and the scientific clinical session should be held at the same time and place, and it is recommended that the present practice be continued without change."

—Agreed that a special committee of five delegates study a recent "management survey" of the "organizational mechanisms" of the A. M. A., and then report back with recommendations. Copies of the survey report are to be sent to all delegates.

—Urged that the television and radio industry make "a more careful screening . . . to eliminate offensive or misleading advertising" of patent medicines which invite "listeners to self-treatment of a variety of ailments or conditions."

—Directed that there be an investigation of "the frequency of the indiscriminate use . . . of stimulants such as amphetamine and its derivatives . . . particularly in relation to athletic programs, and take appropriate action through available channels to prevent such abuse."

—Voted to oppose "the establishment of further veterans' facilities for the care of non-service-connected illnesses of veterans."

—Called for "the free and open selection of physicians by federal employees."

—Again went on record "as being vigorously opposed to any continuation of the doctor-draft law, in whole or in part, or in principle, beyond the expiration date of June 30, 1957."

—Condemned "the compulsory assessment of medical men and staff members by hospitals in fund-raising campaigns."

—Voted official praise of the television drama series, "Dr. Hudson's Secret Journal" for its portrayal of medicine and physicians.

—Recommended that the Joint Blood Council, Inc., be designated "as the contracting agency for blood procurement with all government agencies."

—Reiterated its support of the World Medical Association and recommended "that every member of the American Medical Association join the U. S. Committee of the World Medical Association." The adopted resolution noted that "the World Medical Association is the only international medical organization representing the practicing profession in the fields of medical economics and medical education and devoted to protection of the freedom of the practice of medicine."

—Praised the report of the retiring A. M. A. President, Dr. Dwight H. Murray: "In 12 years of hard and arduous work, Dr. Murray has indeed earned a place in Medicine's Hall of Fame."

—Elected Drs. Clark Wescoe of Kansas City, Kan., and Warde B. Allen of Baltimore as members of the Council on Medical Education and Hospitals; Drs. Hoyt B. Woolley of Idaho Falls, Idaho, and Robert L. Novy of Detroit (reelected) to the Council on Medical Service; reelected Dr. Warren W. Furey of Chicago to the Council on Constitution and Bylaws; and reelected H. L. Pearson, Jr. of Coral Gables, Fla., to the Judicial Council.

—Heard Speaker Askey say: "Never in our A. M. A. history have so many votes been cast so decisively for officers and trustees. There can be no question as to your intent."

—Viewed the new A. M. A. television film, "Even for One," which portrays the "human side" of medicine.

In his address, retiring President Murray said: "I make only two appeals to you: Continue to adopt positive programs of action and service for the public, and be prepared to make even greater, far-reaching decisions in the future." In his inaugural address, Dr.

Allman said: "The personality of medicine involves you, the physician, and you, the patient, as individual human beings interested in the scientific advances and complexities of modern medicine."

Other Official Activities

Acclaimed as distinguished guests at the House of Delegates sessions were members of the Woman's Auxiliary of the A. M. A., two representatives of the Student A. M. A., and winners of the National High School Science Fair—Dorothy Lundquist of Webster, S. D., and Warren E. Prince of Hyattsville, Md. Delegates and guests devoted one minute of silence in memory of 37 House members and officers who died in the past year. Joining in the tribute were 10 past-presidents of the A. M. A.

Elected to the presidency of the Woman's Auxiliary of the A. M. A. was Mrs. Paul C. Craig.

Dr. Louis H. Bauer, president of the American Medical Education Foundation, presented more than 20 Awards of Merit to medical societies making outstanding contributions to the AMEF. Brinks' guards escorted representatives of the Illinois Medical Society as they delivered to the rostrum $170,450 in contributions from Illinois members—a record high sum.

Other Meetings

There were scores of other medical meetings held immediately before, during, and after the A. M. A. annual sessions. These included sessions of A. M. A. councils and committees (including civil defense, and medical aspects of automobile injuries and deaths), the Flying Physicians Association, Physicians Art Association, medical alumni groups, state society executives, the American Medical Golfing Association, and many others.

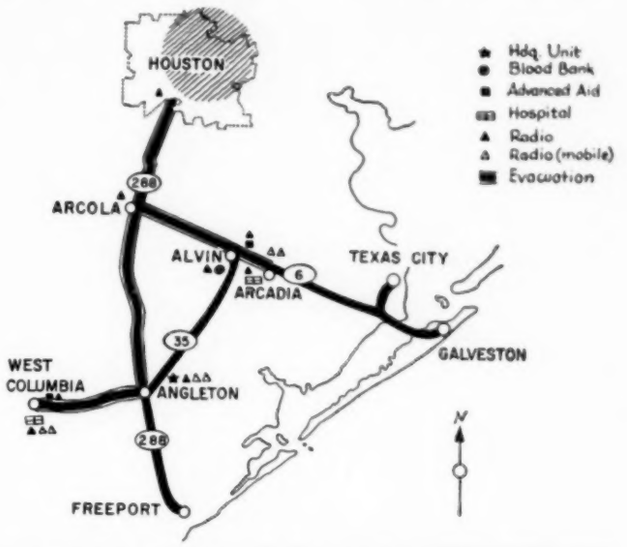
The second annual meeting of the World Medical Association was held June 4 in the Waldorf Astoria, attracting more than 900 members and guests at a business session and at a reception which followed. The W. M. A. has been seeking to establish a central repository for medical credentials and to gain international acceptance of a civil defense emblem to protect medical personnel engaged in civil defense activities.

CIVIL DEFENSE TEST POINTS UP NEED TO PREPLAN EMERGENCY HOSPITAL UNITS

Many U. S. communities may be harboring a false sense of security about their 200-bed emergency hospital units furnished by the Federal Civil Defense Administration. That is the belief of medical monitors who took part in a recent successful test of two of these units—the nation's first such civil defense exercise.

Later this month Dr. Truman G. Blocker Jr. of the University of Texas Medical Branch, who commanded a task force of some 3,000 participants, is scheduled to report findings from the field trial, "Operation Rebound," to the FCDA, the American Medical Association's Council on National Defense, and the committee on MEND (Medical Education for National Defense).

Baylor University College of Medicine, at Houston, Texas, erected one of the emergency hospitals in what it claims to be the record-shattering time of only 55 minutes. But the school's dean, Dr. Stanley W. Olson, points out that, unless there is careful drill and pre-



Survival during disaster is portrayed in a school house in West Columbia, Texas, during the nation's first civil defense exercise involving a 200-bed emergency hospital unit. *Top*, keyed map of test area. *Center*, a makeshift ward for some of the 500 medical students posing as casualties. *Bottom*, a scene in one of three operating rooms of the emergency hospital.

planning, it will take up to a week to set up many of the other 2,000 emergency hospital units which are stored in isolated warehouses in scattered parts of the nation.

Dr. Olson and Dr. John B. Truslow, dean of the University of Texas school, agree that, in order to make most of these hospitals fully usable, equipment and supply deficiencies must be corrected, some of the 256 separate cartons of supplies and equipment must be repackaged and re-stored for more efficient uncrating in a major disaster, and personnel must be trained for teamwork in quick assembly of the material.

"Before our exercise," said Dean Olson, "we spent several days laying everything out. We took inventory to discard nonessentials and obtain omitted items like hypodermic needles and forceps. We repacked functionally, eliminating bulky wrappings and using distinctive color codes and more permanent boxes. Then everything was put into a trailer in reverse order of requirement of items to facilitate unpacking." (New York has taken the lead in preparing for the best immediate use of an emergency hospital unit by arranging component units in assembly-line fashion and scheduling "dry runs" for personnel at regular intervals.)

"We hope that as a result of our program and report some overall plan will be developed for gaining the maximum value from these packaged hospitals," said Dr. Olson. "Perhaps different communities require their own techniques for preparation in time of disaster. Perhaps it is not feasible for the original packing layout to meet special needs of various local civil defense units in all cases. At any event, efficient civil defense depends upon extensive rehearsals with these emergency hospital units, and upon good communications during the rehearsals. In our exercise, communications bogged down under the weight of overload plus interference by amateur radio operators. An emergency radio band should be set aside for civil defense use in the event of disaster."

Each of the FCDA's emergency hospital systems has 200 beds, three fully equipped operating rooms, an emergency room, full sterile and central supply equipment, and laboratory, pharmaceutical, and x-ray departments. The 22½-hour exercise last March 29 and 30 tested hospital units in a grade school at West Columbia and in a tent and quonset hut near Arcadia, 55 miles and 37 miles, respectively, from Houston. Headquarters was established at a highway junction between the two towns.

Among the observers were Dr. Harold S. Diehl, Chairman of the A. M. A. Council on National Defense; Dr. Harold C. Lueth, Chairman of the Council's Committee on Civil Defense; and Council Secretary Frank W. Barton. Also attending were Assistant Secretary of Defense Frank Berry and representatives of the U. S. Public Health Service, American College of Surgeons, Texas Medical Association, 42 medical schools, and the Brazoria, Galveston, Harris, Matagorda, and Wharton County medical societies. Other participants included nursing groups, hospital administrators, the Red Cross, and dental society officials.

"Operation Rebound" assumed that all of Houston's medical facilities and personnel were destroyed within a 300-square-mile area encompassing a nuclear bomb explosion. The estimated 500 injured persons who figured as typical survivors were played by medical students. Their "injuries" were contrived so skillfully with plastics (one "victim" seemed to have an eye dangling from its socket) that medical personnel at first were genuinely shocked by the realism. Radioactive materials were concealed in the clothing of some medical students as a means of providing unrehearsed experience for radiologic monitors whose duties were to prevent contamination of casualties.

"It was a most realistic demonstration," reported the A. M. A. representatives.

SCIENCE FAIR WINNERS

Dwight H. Murray, immediate A. M. A. past-president, presented citations to the winners of the National Science Fair for 1957 at the Biltmore Hotel, Los Angeles, on May 10. The awards were made at a special banquet given by the Association for the 600 participants of the Science Fair.

Winners of the National Science Fair awards for 1957 are (left to right) Robert B. Nathanson and Lillian M. Harris, both honorable mention citation winners, and Dorothy Lindquist and Warren E. Prince, winners of first-place citations. Dr. Murray, immediate past-president of the A. M. A., presented the citations.

Miss Dorothy Lundquist, Webster, S. D., and Warren E. Prince, Hyattsville, Md., won the two first-place citations and a trip to the A. M. A. Annual Meeting in New York City for their exhibits "The Effects of Inadequate Sleep on Physical and Mental Alertness" and "Spray Method for Autogenous Skin Grafts" respectively.

The honorable mention citation winners are Miss Lillian M. Harris, Tucson, Ariz., for her exhibit on "African Sleeping Sickness," and Robert B. Nathanson, West Hartford, Conn., for his display of "Fungistatic Action of Squalene and Certain Unsaturated Fatty Acids on T. rubrum in Vitro."

The National Science Fair, in which the A. M. A. participated for the second consecutive year, is sponsored by Science Service to stimulate interest among high school students in science as a future career.

MEDICAL NEWS

CALIFORNIA

Dr. Hinshaw Lectures in Russia.—Dr. Horton C. Hinshaw, Stanford University School of Medicine, San Francisco, flew to Moscow recently to speak before the U. S. S. R.'s sixth All-Union Congress on Tuberculosis. His paper was entitled "Present Day Treatment of Tuberculosis in the United States." The only American attending the Moscow meetings, he was invited by Prof. F. V. Shebanoff, chief of the organizational committee for the congress. Dr. Hinshaw is head of the Stanford division of chest diseases, has published over 200 articles in his field, and is the author or co-author of several books. He was formerly president of the American Trudeau Society and is currently a director of the San Francisco Tuberculosis Association.

GEORGIA

Personal.—The American Heart Association has announced that Dr. Eugene B. Ferris has been appointed medical director of the association. He formerly served as professor of medicine at Emory University School of Medicine, Atlanta. Prior to assuming his teaching position in Atlanta in 1952, he was professor of medicine at the University of Cincinnati College of Medicine. He has also served as vice-president of the American Heart Association.

Dr. Sydenstricker Honored.—University of Georgia School of Medicine, Augusta, recently honored Dr. Virgil P. Sydenstricker by presenting "V. P. Sydenstricker Day." Dr. Sydenstricker, who has been professor of medicine at the school since 1922, has retired. The program for the day in his honor included a lecture by Dr. William J. Darby, head, department of biochemistry, Vanderbilt University School of Medicine, Nashville, Tenn. Dr. Sydenstricker was recently awarded a grant for the study of collagen diseases. He is recipient of the King's Medal for service to the British Empire, having studied nutrition problems in England in World War II.

ILLINOIS

Chicago

Society News.—At the Annual Meeting of the Metropolitan Dermatological Society of Chicago the following officers were elected: Dr. Cleveland J. White, president; Dr. James I. W. Madura, vice-president; and Dr. Tibor Benedek, secretary-treasurer.

Personal.—Dr. Franklin C. McLean, University of Chicago emeritus professor of physiology, was awarded an honorary degree of doctor of medicine by the University of Lund recently in Lund, Sweden, in a ceremony in the Cathedral of Lund. As part of the award he received a ring, a diploma, a top hat, and a salute of two cannon shots. Dr. McLean, who organized the University of Chicago Clinics and was its first director from 1927 to 1932, retired from the faculty in 1953. Since that time he has remained at the University to continue his research on the physiology of bone.

Professor Kimmel Comes to Chicago.—Prof. Donald L. Kimmel, Ph.D., professor of anatomy, Temple University, has been appointed professor and chairman, department of anatomy, Chicago Medical School. Dr. Kimmel has been a member of the faculty of the University of Michigan and Louisiana State University, and has been associated with Temple University since 1944. He is the author of 32 papers and other publications having to do with neuroanatomy and physiology. Since 1927 the position of professor and chairman, department of anatomy at the school has been held by Dr. John J. Sheinin, now president of the school. Because of his expanding responsibilities, it was necessary to appoint a full-time professor.

INDIANA

Society News.—The officers of the Indiana Roentgen Society for the coming year are: president, Dr. Arthur A. Hobbs, Evansville; vice-president, Dr. Wallace D. Buchanan, South Bend; secretary-treasurer, Dr. Chester A. Stayton Jr., Indianapolis.

IOWA

Ciba Award to Professor Halmi.—Nicholas S. Halmi, associate professor in the department of anatomy at the State University of Iowa, Iowa City, was presented the 1957 Ciba award of the Endocrine Society for outstanding research in human endocrine glands, particularly in the areas of the interrelationships between the brain and the glands of internal secretion. The presentation was made during the 39th annual meeting of the Endocrine Society held in New York City recently. Sponsored by Ciba Pharmaceutical Products Inc., the award is made each year to a scientist 35 years of age or under who, in the opinion of the society, has made a notable contribution in the field of endocrinology. The award of $2,500 will be used by Dr. Halmi to broaden his current research work and to collaborate as a visiting investigator in other laboratories.

KENTUCKY

University News.—A grant of $10,000 has been made to the department of pediatrics of the University of Louisville School of Medicine by the Courier-Journal and Louisville Times Foundation. The grant is to be used by Dr. Frank Falkner in a study of identical twins as part of the work of the department's child-development unit.

Dr. and Mrs. McClure Pass State Bar.—Dr. G. David McClure, Louisville ophthalmologist, and his wife, Mrs. Gwendolyn Parker McClure, a former teacher, have

---

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

passed the state bar examinations. The McClures, who have been studying law at night at the University of Louisville School of Law, were among 36 who took the exams in early March. Doctor McClure was graduated from the University of Louisville School of Medicine in 1946, interned at St. Joseph Infirmary, Louisville, and did graduate work at St. Louis. Mrs. McClure holds a master's degree in chemistry from the University of Louisville and has taught school near each post where her husband has been stationed, including his military assignments from 1950 to 1953.

LOUISIANA

Society News.—The following officers of the New Orleans Graduate Medical Assembly were recently elected: Dr. Charles L. Brown, president; Dr. Joseph O. Weilbaecher Jr., president-elect; Dr. Max M. Green, first vice-president; Dr. Joseph N. Ane, second vice-president; Dr. Milton M. Hattaway, third vice-president; Dr. Maurice E. St.Martin, secretary; and Dr. Ralph M. Hartwell, treasurer. The 21st annual meeting of the assembly will be held March 3-6, 1958, headquarters at the Roosevelt Hotel.

MASSACHUSETTS

Thomas Linacre Award.—Drs. Roy J. Heffernan, and William A. Lynch, are the recipients of the Thomas Linacre award for their joint effort, "Is Therapeutic Abortion Scientifically Justified?" judged best by a special editorial board appointed to review the articles written by Catholic physicians and published in *The Linacre Quarterly* during the past five years. Both recipients are practicing physicians in Boston and are members of the Guild of St. Luke. The award presentations were made at the dinner meeting of the silver jubilee celebration observing the 25th anniversary of the Federation of Catholic Physicians' Guilds.

MISSISSIPPI

Society News.—At the recent annual session of the Mississippi State Medical Association the following officers were elected: president, Dr. Howard A. Nelson, Greenwood; president-elect, Dr. Guy T. Vise, Meridian; vice-presidents, Drs. John C. Russel, Cleveland, Lynn D. Abernethy, Jackson, and Gilliam Swink Hicks, Natchez; and treasurer, Dr. Omar Simmons, Newton.

NEW YORK

Personal.—Dr. Paul J. Christenson, formerly Utica health commissioner has been appointed to the medical staff of the Norwich Pharmacal Company and Eaton Laboratories. Dr. Christenson was in general practice at Averill Park from 1949 to 1952 and later had charge of a three-county health department in Virginia, with headquarters at Coveington.

Dr. Berson Honored.—Dr. Solomon A. Berson, chief, radioisotope service, Veterans Administration Hospital, Bronx, was presented the first Lilly award at the annual banquet of the American Diabetes Association recently during the 17th annual meeting. The annual award, supported by Eli Lilly and Company, consists of $500 and a gold medal. Its purpose is to recognize demonstrated research in the field of diabetes, taking into consideration independence of thought and originality.

Mental Hygiene Department Appointments.—Four major administrative posts in the New York State Department of Mental Hygiene will be filled July 1. Dr. Arthur G. Rodgers, director of Binghamton State Hospital, will become director of Syracuse State School; Dr. Ulysses Schutzer, assistant director of Central Islip State Hospital, will succeed him as director of Binghamton. Dr. Charles Greenberg, director of Craig Colony, will become senior director of Rome State School and succeeding him as director at Craig Colony will be Dr. William C. Johnston, assistant director of Matteawan State Hospital. Dr. Rodgers, who has been director at the Binghamton hospital since Jan. 1, 1953, will succeed Dr. Lloyd E. Watts who has been serving as acting director since the retirement of Dr. Sidney W. Bisgrove.

New York City

Hospital News.—In commemoration of its 100th anniversary, Lenox Hill Hospital recently presented a four-day program of celebration, including a panel discussion between science writers and hospital staff members and scientific and historical exhibits. An anniversary reception and dinner were also held, at which distinguished service medals were presented by Mr. C. Otto von Kienbusch and Mr. Theodore F. Childs to hospital staff members.

Society News.—At the New York Academy of Gastroenterology annual meeting, the following officers were elected for 1957-58: president, Dr. Jerome A. Marks; president-elect, Dr. Milton J. Matzner; first vice-president, Dr. Michael Weingarten; second vice-president, Dr. Joseph R. Van Dyne; secretary, Dr. Alexander Slanger; recording secretary, Dr. Jerome Weiss; treasurer, Dr. William C. Jacobson; and chairman, board of trustees, Dr. Harry Barowsky.

Establish AOA Chapter.—A chapter of Alpha Omega Alpha was installed at New York Medical College, Flower and Fifth Avenue Hospitals, recently. Dr. Willard C. Rappleye, vice-president of Columbia University and dean of the College of Physicians and Surgeons, made the installation address on "The Role of Scholarship in Present Day Medicine." Dr. Josiah J. Moore, national secretary-treasurer of Alpha Omega Alpha, installed the chapter and presented keys and certificates. The 24 charter members included six faculty members, and 18 students, including Dr. J. A. W. Hetrick, president; Dr. Ralph E. Snyder, dean; Dr. Linn J. Boyd, Dr. Lois C. Lillick, Dr. Lawrence B. Slobody, and Dr. James M. Winfield, department directors.

NORTH CAROLINA

Personal.—Dr. Tihamer Z. Csaky, associate professor of pharmacology, University of North Carolina School of Medicine, Chapel Hill, has been granted a Guggenheim Fellowship for research study. He will go to Copenhagen, Denmark, next spring to work with

Prof. Hans Ussing at the Institute of Biological Isotope Research in the field of mechanisms of active transport in biological systems.

Cancer Research Grant.—Edward C. Horn, Ph.D., associate professor of zoology, Duke University, has been awarded a three-year cancer research grant of $30,000 by the National Cancer Institute, a subdivision of the U. S. Public Health Service. The research is the investigation of antisera. Earlier investigation leading up to the new grant was done by Dr. Horn under other U. S. Public Health Service grants with the work being conducted in the Biology Division of the Oak Ridge National Laboratory.

University News.—The National Institute of Allergy and Infectious Diseases of the U. S. Public Health Service has granted $94,010 to Dr. William J. Cromartie, of the University of North Carolina School of Medicine. The money will be used for a five-year study of bacterial infections of the kidney. Specific objectives of the proposed studies are the development of precise methods of diagnosing chronic infections of the kidney, determining the relative importance of such infections as a cause of kidney failure and high blood pressure, and determination of the best methods of treating chronic infections of the kidney.

OKLAHOMA

Society News.—The Oklahoma Tuberculosis Association recently changed its address to P. O. Box 3303, Oklahoma City 5.

Personal.—Dr. Carl Puckett, Oklahoma City, managing director of the Oklahoma Tuberculosis Association, recently received the Richard Burke award, which is given each year to the person who has provided "outstanding service" to the state recovery club and in the field of tuberculosis.

PENNSYLVANIA

Philadelphia

Harry E. Bacon Foundation.—Recently Dr. Harry E. Bacon, head, department of colon and rectal surgery, Temple University School of Medicine was honored in that the Harry E. Bacon Proctologic Residents Research Foundation was established by his former residents and fellows. The purposes of the organization are to aid financially in research problems referable to the rectum and colon, to supplement income of needy residents, to present awards for original work performed, and to establish a residents' travel fund to visit surgical clinics. Dr. Bacon was also recently accorded honorary fellowship in the Cuban Society and the Mexican Surgical Society.

University News.—One of the four original M.D. diplomas granted by the University of Pennsylvania in 1771 has been presented to the University for its archives, it was announced recently. The diploma was awarded to Jonathan Elmer, a member of the first graduating class in medicine. It was presented to the University by his great-great grandson, Dr. Walter Gray Elmer, also an alumnus. Dr. Jonathan Elmer was one of 10 graduates of the first class in medicine of the college which became the Medical Department of the University of Pennsylvania. This School of Medicine was founded in 1765. On June 1, 1768, Dr. Elmer and his classmates received the degree of bachelor of medicine. Four of this group, including Dr. Elmer, continued their studies and in 1771 received the degree of doctor of medicine.

Dr. Walter Gray Elmer was graduated from the University School of Medicine in 1897. He was a faculty member in the School of Medicine for many years and later was a professor of orthopedics in the Graduate School of Medicine, University of Pennsylvania, being made professor emeritus in 1941.

RHODE ISLAND

Society News.—Officers of the Rhode Island Medical Society for 1957-1958 include the following: president, Dr. George W. Waterman, Providence; president-elect, Dr. Francis B. Sargent, Providence; vice-president, Dr. Stanley Sprague, Pawtucket; secretary, Dr. Thomas Perry Jr., Providence, and treasurer, Dr. John A. Dillon, Providence.

TENNESSEE

Society News.—At the annual meeting of the Tennessee State Medical Association held recently the following officers were elected: president, Dr. Jesse Paul Baird, Dyersburg, succeeding Dr. Robert B. Wood, Knoxville; president-elect, Dr. James C. Gardner, Nashville; and Drs. Thurman Shipley, Cookeville, Moore J. Smith, Chattanooga, and Byron O. Garner, Union City, vice-presidents.

TEXAS

Postgraduate Medical Assembly.—The 23rd annual session of the Postgraduate Medical Assembly of South Texas will be held at the Shamrock Hilton, July 15-17. Three sections, medical, surgical, and ophthalmological-otolaryngological, meeting simultaneously will present a total of 66 medical lectures. Intermission periods in the surgical and medical sections permit the attendance of a total of 30 lectures in these two sections. The registration fee of $20.00 includes all features: scientific program; exhibits, medical motion pictures, three luncheons in the Shamrock Hilton's Emerald Room, entertainment the evening of July 16, and a fashion show tea for the ladies Tuesday afternoon, July 16. For information write the Postgraduate Medical Assembly of South Texas, 412 Jesse H. Jones Library Building, Houston 25, Texas.

Medical Scholarships Fund.—The late Dr. Samuel E. Thompson, who died at Kerrville last year, has left the bulk of his $500,000 estate as a loan fund for students at the University of Texas Medical Branch in Galveston. Dr. Thompson was a former president of the Texas Medical Association. Under stipulation of the will, the money is to be used "to assist poor and deserving young men and women students, citizens of the State of Texas who without such assistance might not be able to obtain the advantage of a medical education." The loans will not exceed $3,000 per student

and will be made at a rate of interest not to exceed four per cent. Other details of the fund are to be worked out by the trustees. It was known last January that Dr. Thompson had made a $50,000 bequest to the Texas Memorial Medical Library at Austin.

GENERAL

New Journal of Cardiology.—In January, 1958, publication will begin of the official organ of the American College of Cardiology, to be entitled *The American Journal of Cardiology*. Editor of the new journal will be Dr. Simon Dack, of New York. The publication will be devoted to clinical cardiology. Monthly departments on "What is New in Cardiology" will be included.

International Society of Psychopharmacology.—At the recent Symposium on Psychotropic Drugs in Milan, Italy, it was tentatively decided to form an International Society of Psychopharmacology, comprising the disciplines of psychiatry, pharmacology, neurophysiology, and psychology. An organizational meeting will be held during the International Congress for Psychiatry in Zurich Sept. 1-7. For information write Dr. Herman C. B. Denber, Director of Psychiatric Research, Manhattan State Hospital, Ward's Island, New York City 35, N. Y.

Bats and Rabies.—Recently the discovery has been made that ordinary insectivorous bats of this country may become infected and transmit rabies to human beings by bitting them. One recorded victim was a Texan woman, in October, 1951. Another recorded case was that of a Floridian boy, in June, 1953. Prompt recognition by the boy's father and by the health officer of the danger, and the administration of the Pasteur treatment, saved the boy's life. Two patients were reported in Pennsylvania. Both received prompt diagnosis, confirmed by laboratory examination of the bat's brain in the second.

Summer School of Alcohol Studies.—The 15th annual session of the Summer School of Alcohol Studies will be presented at Yale University, New Haven, Conn., July 1-27. Lectures and seminars will be held under the direction of specialists drawn from the social sciences, medicine and psychiatry, religion, education, and public health. The program presents an interdisciplinary study of the problem of alcohol and alcoholism in society. Workshops for physicians, caseworkers, psychologists, and other professional persons are scheduled. Enrollment is limited to 200. For information write Yale Summer School of Alcohol Studies, 52 Hillhouse Ave., New Haven, Conn.

National Lupus Erythematosus Foundation.—Establishment of the National Lupus Erythematosus Foundation, Inc. was announced recently by Dr. Edmund L. Dubois, chairman of the medical advisory board for the foundation. During the past seven years 225 patients with systemic lupus erythematosus were treated at the Los Angeles General Hospital. Because of its close relationship to rheumatoid arthritis, it is believed that the incidence of lupus erythematosis will become a more significant field for research. The foundation was formed to support basic and clinic research on both systemic and discoid lupus erythematosis. Initially contributions will be used to continue these studies and to support fundamental biochemical research. The foundation is incorporated in California as a nonprofit organization. Information concerning the foundation and its activities may be obtained from Dr. Edmund L. Dubois, National Lupus Erythematosis Foundation, Inc., 341 South Vermont Ave., Los Angeles 5.

Moon Eye Research Foundation.—Because he himself developed glaucoma which eventually made him blind 11 years ago, Mr. Thomas E. Moon of Philadelphia, a Western Electric executive engineer became interested in the restoration of sight in people blinded by clouded corneas. He has succeeded in having made an instrument to hold the cornea in place and keep it from collapsing during operation. The instrument has been used successfully in animals, but has not yet been used on a human being. In order to perfect this and other means of doing corneal transplants successfully, the Marguerite Barr Moon Eye Research Foundation, Inc., has been organized. Its headquarters are in Winston-Salem. On the board of directors are Mr. Moon and three other Western Electric engineers and two ophthalmologists, Dr. Turgut N. Hamdi, of Philadelphia, and Dr. Lawrence B. Holt, of Winston-Salem. The foundation has the assurance of a total of $41,682 in grants from the U. S. Department of Health, Education and Welfare, to be distributed over 1957, 1958, and 1959. Trust funds are also being contributed.

Psittacosis.—The morbidity and mortality report of the U. S. Public Health Service for May 24 states that a case of psittacosis was reported in a veterinarian who worked in a poultry processing plant in Pennsylvania. The patient presented typical symptoms and had a complement fixation titer of 1:32. Since a number of persons working in the plant were reported ill at the same time, a serologic survey was made, blood specimens being collected from 89 employees. There were reactions in 12 persons; 3 had titers of 1:32 and the others had titers of 1:8. The 12 persons worked in various departments of the plant, which processes chickens, ducks, turkeys, geese, and pigeons. The exact source of infection was not established.

Three other cases in Pennsylvania involved a local health department worker (complement fixation titer, 1:64), a woman who owned a parakeet (x-ray revealed patchy pneumonitis in the right lower lobe of the lung; complement fixation titer rose from 1:50 to 1:320 on blood specimens collected two weeks apart), and the woman's husband (x-ray revealed a localized consolidation in the right lower lobe).

The California State Department of Public Health has reported two cases of psittacosis, one in a woman employed in a pet shop and the other in a man exposed to pigeons. The Indiana State Board of Health has reported two cases in employees of a department store. Both were selling parakeets.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	May 25, 1957		May 25, 1956 Total
	Paralytic Type	Total Cases Reported	
New England States			
Maine	....	....	....
New Hampshire	....	....	....
Vermont	1	1	....
Massachusetts	....	....	....
Rhode Island	....	....	....
Connecticut	....	....	....
Middle Atlantic States			
New York	1	1	3
New Jersey	....	....	....
Pennsylvania	....	....	4
East North Central			
Ohio	....	....	3
Indiana	....	....	....
Illinois	....	2	7
Michigan	....	1	3
Wisconsin	....	....	1
West North Central States			
Minnesota	....	....	....
Iowa	....	....	4
Missouri	2	3	2
North Dakota	....	....	....
South Dakota	....	....	....
Nebraska	1	4	2
Kansas	....	....	....
South Atlantic States			
Delaware	....	....	1
Maryland	....	....	....
District of Columbia	....	....	....
Virginia	1	1	....
West Virginia	....	....	....
North Carolina	1	3	1
South Carolina	2	2	1
Georgia	1	1	....
Florida	....	1	1
East South Central States			
Kentucky	....	....	2
Tennessee	....	....	3
Alabama	....	2	2
Mississippi	....	....	3
West South Central States			
Arkansas	....	....	....
Louisiana	....	1	7
Oklahoma	....	....	2
Texas	14	18	32
Mountain States			
Montana	....	....	....
Idaho	....	....	....
Wyoming	....	....	....
Colorado	1	2	....
New Mexico	....	....	1
Arizona	....	....	....
Utah	....	4	....
Nevada	....	....	....
Pacific States			
Washington	....	....	....
Oregon	1	1	2
California	6	12	25
Territories and Possessions			
Alaska	....	....	....
Hawaii	....	....	....
Puerto Rico	....	....	1
Total	32	60	113

Fellowships in Biometry and Epidemiology.—The Yale University Graduate School, New Haven, Conn., recently announced the availability of American Cancer Society predoctoral and postdoctoral fellowships. Applicants for the former must have the B.A. or B.S. degree and are expected to enter the graduate school as candidates for the Ph.D. degree. They will receive training in one or more fields of biology and statistics. Fellowships are for three years; stipends, $2,000 a year. Additional funds may be available. Applicants for postdoctoral fellowships must have either an M.D., a Ph.D., or an Sc.D. degree. These fellowships are for younger investigators, or for more mature men and women who want to extend their fields of competence. In addition to carrying out their own research, fellows will be given training in biometry, biostatistics, and other selected subjects. Fellowships are for one year, but may be renewed for two more. Stipends are $4,000, and increase, depending on individual circumstances. For information, write to Prof. E. Cuyler Hammond, Director of Graduate Studies in Biometry, 30 Hillhouse Ave., Yale University, New Haven, Conn. Application blanks for predoctoral fellowships may be obtained from the Director of Admissions, Graduate School, Yale University, New Haven, Conn.

Society News.—At the recent meeting of the **Association of University Radiologists,** the following officers were elected: president, Dr. Roger A. Harvey, department of radiology, University of Illinois College of Medicine, Chicago; president-elect, Dr. David M. Gould, department of radiology, University of Arkansas Medical Center, Little Rock; and secretary-treasurer, Dr. Paul Riemenschneider, department of radiology, Syracuse University College of Medicine, Syracuse, N. Y.——At the meeting of the **American Laryngological Association** held in Washington, D. C., recently the following officers were elected: president, Harry P. Schenck, Philadelphia; first vice-president, Francis E. LeJeune, New Orleans; second vice-president, Pierre P. Viole, Los Angeles; secretary, James H. Maxwell, Ann Arbor, Mich.; treasurer, Fred W. Dixon, Cleveland; editor and historian, Edwin N. Broyles, Baltimore.——At the recent meeting of the **American Urological Association,** the following officers were elected: president, Dr. William J. Baker, Chicago; president-elect, Dr. Adolph A. Kutzmann, Los Angeles; secretary, Dr. Samuel L. Raines, Memphis, Tenn.; and treasurer, Dr. Grayson L. Carroll, St. Louis. The 1958 meeting will be held in New Orleans, April 28-May 1, with headquarters at the Roosevelt Hotel.

Markle Foundation Fellowships.—The National Academy of Sciences–National Research Council has announced the selection of 10 scientists to be awarded fellowships in the medical sciences for the coming academic year under the sponsorship of the John and Mary R. Markle Foundation. The recipients and their programs of study are as follows:

Mrs. Olga O. Blumenfeld, Tarrytown, enzymatically active modified pepsin resulting from autodigestion.

Dr. Bernard A. Cooper, Westmount, Quebec, Canada, mode of action of the "intrinsic factor" in the absorption of vitamin B_{12}.

Mr. Maynard M. Dewey, Hickory Corners, Mich., parotid gland after removal of the hypophysis.

Dr. Gerald H. Holman, Winnipeg, Canada, distribution of radioactive steroids in human plasma and the biosynthesis of steroids in adrenal hyperplasia.

Mr. Emmett J. Johnson, Baton Rouge, Louisiana, localization of oxidative phosphorylation in Mycobacterium tuberculosis.

Dr. Frederic Kavaler, New York City, cardiac excitability as related to ion movements.

Mr. Jack L. Kostyo, Elyria, Ohio, hormonal and chemical regulation of uterine muscle metabolism.

Mr. Franklin R. Leach, Cisco, Texas, enzymatic mechanism of α-keto acid decarboxylation.

Mr. Royce Z. Lockart Jr., Seattle, biological significance of inactive virus in the L-cell-western equine encephalitis virus host-cell system.

Dr. Edward S. Reynolds Jr., Marblehead, Mass., changes in the metal content of the liver associated with disease.

FOREIGN

International Poliomyelitis Conference.—Medical scientists, physicians, and surgeons from more than 50 nations will meet in Geneva, Switzerland, July 8-12 to discuss a world-wide assault on poliomyelitis at the Fourth International Poliomyelitis Conference under the auspices of the International Poliomyelitis Congress. Basil O'Connor, president of the U. S. National Foundation for Infantile Paralysis, is also president of the Congress. The meeting will open on the morning of July 8 with reports of the official delegates on the nature of the polio problem in their respective nations. The next session will be devoted to a discussion of American experience with the Salk vaccine, with Dr. Jonas E. Salk, University of Pittsburgh, speaking on "Basic Principles Underlying Vaccination with Inactivated Viruses." Other speakers at this session will be Dr. David Bodian, Johns Hopkins University, and Dr. Alexander D. Langmuir, U. S. Public Health Service. Dr. Jeppe Ørskov of the Danish State Serum Institute, Copenhagen, will preside. On July 9 the speakers will be Dr. Hilary Koprowski, director Wistar Institute of Philadelphia; Dr. Albert B. Sabin, University of Cincinnati; Dr. John P. Fox, Tulane University; and Dr. Anthony M. M. Payne, World Health Organization, Geneva, Switzerland. Dr. James H. S. Gear, South African Institute for Medical Research, Johannesburg, will preside at this second session. Subsequent sessions will deal with the newest medical and surgical methods of treating polio, with virus diseases resembling polio, and with basic researches into the nature of viruses and their interaction with living cells.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

CALIFORNIA: *Written Examination.* Los Angeles, Aug. 19-22; Sacramento, Oct. 21-24. *Oral Examination.* Los Angeles, August 17; San Francisco, Nov. 16. *Oral and Clinical for Foreign Graduates.* Los Angeles, Aug. 18; San Francisco, Nov. 17. Sec., Dr. Louis E. Jones, 1020 N St., Sacramento 14.

CONNECTICUT:* *Regular. Examination.* Hartford, July 9-11. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

DELAWARE: *Examination.* Dover, July 9-11. *Endorsement.* Dover, July 18. Sec., Dr. Joseph S. McDaniel, 225 S. State St., Dover.

FLORIDA:* *Examination.* Miami, June 23-25. Sec., Dr. Homer L. Pearson, 901 N. W. 17th St., Miami.

GEORGIA: *Examination and Reciprocity.* Augusta and Atlanta, June. Sec., Mr. Cecil L. Clifton, 111 State Capitol, Atlanta 3.

IDAHO: *Examination and Reciprocity.* Boise, July 8-10. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

MAINE: *Examination and Reciprocity.* August, July 9-11. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: *Examination and Endorsement.* Boston, July 9-12. Sec., Dr. Robert C. Cochrane, 37 State House, Boston 33.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

MISSISSIPPI: *Examination.* Jackson, June 24-25. *Reciprocity.* Jackson, June 26. Asst. Sec., Dr. R. N. Whitfield, Old Capitol, Jackson.

MONTANA: *Examination and Reciprocity.* Helena, Oct. 1-2. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEW HAMPSHIRE: *Examination and Reciprocity.* Concord, Sept. 11-13. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW YORK: *Examination.* Albany, Buffalo, New York, Rochester and Syracuse, July 9-12. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany 7.

NORTH CAROLINA: *Endorsement.* Bowling Green, July 26. *Written Examination.* Raleigh, June 17-20. Sec., Dr. Joseph J. Combs, Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 10-13, *Reciprocity.* Grand Forks, July 13. Sec., Dr. C. J. Glaspel, Grafton.

OREGON:* *Examination and Reciprocity.* Portland, July 10-11. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July 10-12. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, June 27-28. Admin. of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, June 25-26. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination and Reciprocity.* Place not yet determined, July 16-17. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 24-26. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, July 11-13. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

WASHINGTON:* *Examination.* Seattle, July 15-17. Sec., Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN:* *Examination.* Milwaukee, July 9-11. Sec., Dr. Thomas W. Tormay, Jr., 1140 State Office Bldg., Madison 2.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

HAWAII: *Examination.* Honolulu, July 8-9. Sec., Dr. I. L. Tilden, 1020 Kapiolana St., Honolulu.

PUERTO RICO: *Examination.* San Juan, September 4. Sec., Mr. Joaquin Mercado Cruz, Box 9156, Santurce.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

COLORADO: *Examination and Reciprocity.* Denver, Sept. 4-5. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

OKLAHOMA: *Examination.* Oklahoma City, Sept. 27-28. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

TENNESSEE: *Examination.* Memphis, July 2-3. Sec., Dr. O. W. Hyman, 62 South Dunlap St., Memphis 3.

---

*Basic Science Certificate required.

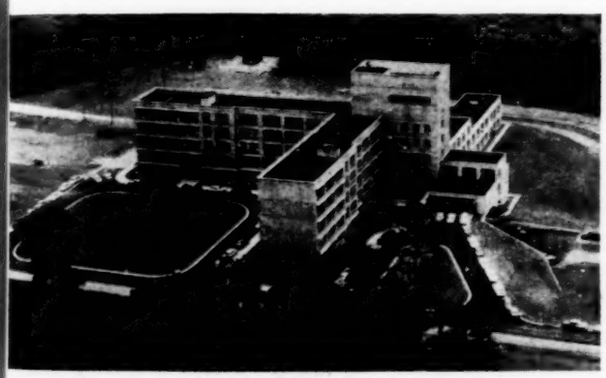
GOVERNMENT SERVICES

ARMY

New Hospital at Fort Belvoir.—The new 250-bed Army hospital at Fort Belvoir, Va., which admitted its first patients on May 24, has the newest features of construction and the latest equipment to help insure that patients receive the best care possible. The building could accommodate 300 patients without alteration, and, if necessary, with additions, could be expanded to a 500-bed capacity.

The Fort Belvoir hospital cost about $4,700,000. It is one of seven in an Army modernization program authorized by Congress in 1953. Other hospitals ranging in capacity up to 1,000 beds are in various stages of planning; five are in various stages of construction. The Engineer Corps has under contract 17 new hospitals for the Air Force both overseas and in this country.

Fort Belvoir's new structure, replacing a rambling series of World War II cantonment-type frame buildings, is a six-story reinforced concrete and brick build-



U. S. Army Hospital; Fort Belvoir, Va.

ing on a 20-acre tract, located on Belvoir Road and 12th Street, near U. S. Highway no. 1. Constructed along the newest lines in hospital design, the building will have all bed spaces on the top five floors. No ward or room is more than a few steps from the nearest elevator.

The new hospital, named after the late Brig. Gen. Wallace DeWitt, has the latest communication devices. Each of the bed spaces in the 9 wards and 53 private and semiprivate rooms is equipped with an audio system of communication which enables the patient and nurse to converse while the latter remains at her station. Another new communication feature is a central dictating system which enables the doctor to examine the patient, prescribe for him, and then immediately make his report. He simply picks up an instrument in the ward office and dictates the report into a central receiving station where it is recorded, typed, and returned to the ward station in a short time. This eliminates the old chore of writing the record longhand. A pneumatic-tube system connects each of 46 stations, offices, and departments of the hospital, making it possible to dispatch prescriptions, papers, and other small items to any part of the building in 90 seconds.

Another feature is a pipe system making oxygen available to each of the wards and to private and semiprivate rooms. All of the oxygen supply is kept in a central area. The hospital also has a central sterilization room. For the isolation ward, there is a double kitchen—one for serving the food to patients and the other for handling the dishes, trays, and utensils which have been used by patients. Other wards have standard ward food service kitchens, each of which is equipped with an ice-making machine, refrigerator, steam tables, hot plates, and automatic dish washer.

Every ward and room is equipped with a television receiver and a radio system. Each bed is equipped with a pillow receiver so that the programs will not disturb other patients. Three of the wards, the five operating rooms, the surgical staff lounge, and the laboratories and clinics are air-conditioned.

In addition to furnishing medical service to personnel and their families stationed at Fort Belvoir, the new hospital will provide inpatient and outpatient care for military personnel from the Pentagon, Fort Myer, Vint Hill Farms, and A. P. Hill Military reservation.

Maintenance and upkeep costs are expected to be considerably lower than they were in the old hospital. Col. Charles L. Kirkpatrick, who has been commanding officer of the old hospital, will continue in the same capacity in the new medical center.

VETERANS ADMINISTRATION

Residency in Physical Medicine.—The VA Hospital at Houston, Texas, offers a three-year approved residency in physical medicine and rehabilitation. The program is closely affiliated with Baylor University College of Medicine and its other affiliated hospitals. The residency is available in either the regular or career type of appointment. The regular residency has a stipend range from $2,840 to $3,550 per annum; the career type carries a staff-status salary, which ranges from $5,915 to $8,990 per annum, with an obligation to serve the Veterans Administration for a specific period after completion of the residency (e.g., two years of obligated service for three years of residency). For further information, write Dr. Lewis A. Leavitt, Chief, Physical Medicine and Rehabilitation Service, VA Hospital, Houston, Texas.

Residencies in Psychiatry.—The VA Hospital, Lyons, N. J., announces the availability of one-to-three-year residencies in psychiatry that are fully accredited by the American Board of Psychiatry and Neurology. The training program consists of lectures, conferences, and seminars, under the direction of the department of psychiatry of New York Medical College. In addition to intensive training intramurally and through rotation in special hospitals and clinics in the vicinity, the hospital sponsors an annual institute and a series of guest lecturers. Training may commence at any time, according to Dr. M. P. Rosenblum, director of professional education.

DEATHS

Emerson, Haven, New York City, professor emeritus of public health practice at Columbia University College of Physicians and Surgeons, died in a hospital at Greenport, N. Y., May 21, aged 82. Born in New York City Oct. 19, 1874, he was the son of Dr. John Haven Emerson, one of the city's first public health physicians, and a grandnephew of Ralph Waldo Emerson. Following graduation from the Columbia University College of Physicians and Surgeons in 1899, Dr. Emerson served an internship at the Bellevue Hospital, where he was later assistant visiting physician. For many years he was a member of the teaching faculty at his alma mater, where in 1922 he became professor of public health practice and director of the Delamar Institute of Public Health, retiring in 1940. He was at one time professor of hygiene and preventive medicine at Cornell, lecturer at the Teachers College, Columbia University, and at the New York School of Social Work, visiting lecturer at the School of Public Health, University of Michigan, and visiting professor of public health at the University of Minnesota School of Public Health. In 1914-1915 he was sanitary superintendent and deputy commissioner, from 1915 to 1917 commissioner of health and president, and for many years a member of the New York City Board of Health. During World War I, he was assigned as chief epidemiologist with the American Expeditionary Forces and for his military service was made Chevalier of the Legion of Honor by France and received the Distinguished Service Medal from his own government. In 1920-1921 he was medical adviser and assistant director of the bureau of war risk insurance in the U. S. Treasury Department. In 1929 he made a survey of health and sanitation in Athens, Greece, for the health section of the League of Nations and had made similar surveys for many cities in this country. A survey of New York City hospitals he directed from 1935 to 1937 led to the formation of the Hospital Council of Greater New York. In 1949 he was given a special Lasker award by the American Public Health Association "for extraordinary achievement in developing a program of complete local health service in every area of the U. S." The American Public Health Association, of which he was president in 1933-1934, awarded him the William Thompson Sedgwick Medal for distinguished service in public health in 1935. At various times he was a member of the National Advisory Health Council, treasurer of the National Health Council, and a member of the commission of expert statisticians of health of the health section of the League of Nations. In 1941-1942 Dr. Emerson was chairman of the Section on Preventive and Industrial Medicine and Public Health of the American Medical Association, of which he was an associate member. He became an honorary fellow of the Royal Sanitary Institute of England in 1934 and was a member of the Association of American Physicians. As health commissioner Dr. Emerson established rigid standards for public health officers in an effort to control epidemic diseases. His efforts led to the formation in 1917 of a committee of the Public Health Association, which, under his chairmanship published a widely circulated report "Control of Communicable Diseases." Dr. Emerson had edited seven editions of the report, which was translated into many languages and accepted as an official standard by many governments. He was the editor of "Alcohol and Man," "The Baker Memorial," "Administrative Medicine," and "Local Health Units for the Nation"; one of the editors of "How to Live"; author of "Alcohol: Its Effects on Man." On Oct. 19, 1949, "Selected Papers of Haven Emerson" was published on the occasion of his 75th birthday by the W. K. Kellogg Foundation, Battle Creek, Mich., of which he was a trustee. In 1937 he received an honorary doctor's degree at the hundredth anniversary of the University of Athens, and he received an honorary doctor of science degree from Columbia in 1954.

Adams, William Milton ✱ Memphis, Tenn.; born in Ripley, Miss., April 26, 1905; Tulane University of Louisiana School of Medicine, New Orleans, 1930; associate professor of surgery at the University of Tennessee College of Medicine, where he was head of the plastic surgery department; founder member and chairman of the American Board of Plastic Surgery, of which he was vice-chairman in 1955; secretary, 1950-1951, president, 1953-1954, American Society of Plastic and Reconstructive Surgery; past-president of the Tennessee Society of Plastic Surgeons; member of the British Association of Plastic Surgeons, American Association of Plastic Surgeons, Southeastern Surgical Congress, and the American Association for the Surgery of Trauma; member of the first International Congress of Plastic Surgery; fellow of the International College of Surgeons and the American College of Surgeons; in 1945 was "Man of the Year" of Kappa Sigma Fraternity; associate editor of *Plastic and Reconstructive Surgery*; founder and director of the Memphis Cleft Lip and Cleft Palate Center in 1950; chief of the department of plastic surgery, John Gaston, Baptist, Methodist, Memphis Eye, Ear, Nose and Throat, St. Joseph, and LeBonheur Children's hospitals; consulting plastic surgeon at the Veterans Administration Hospital and U. S. Public Health Service Hospital; served as chief of surgery and chief of staff at the Methodist Hospital, where he died April 4, aged 51, of coronary occlusion.

Bittenbender, Glace Edward ✱ Jackson, Miss.; born in Nescapeck, Pa., March 2, 1912; New York University College of Medicine, 1943; professor of anesthesiology, University of Mississippi Medical Center; formerly clinical associate professor of anesthesiology at Baylor University College of Medicine in Houston; specialist certified by the American Board of Anesthesiology; certified by the National Board of Medical

✱ Indicates Member of the American Medical Association.

Examiners; an honorary member of the American Society of Anesthesiologists; a member of the Society of University Anesthesiologists, and the Mississippi Society of Anesthesiologists; served as chairman of the section on anesthesiology of the Southern Medical Association; a member of the board of governors of the American College of Anesthesiologists; veteran of World War II; formerly associate director of anesthesiology at the Charity Hospital of Louisiana, New Orleans, where he took his residency training; director of anesthesiology at the University Hospital; served on the staffs of St. Joseph's and Texas Children's hospitals, and the Veterans Administration Hospital in Houston, Texas, where he died April 15, aged 45, of carcinoma of the lung.

White, Arthur Jay, Rear Admiral, U. S. Navy, retired, Baltimore; born in Leipsic, Ohio, Nov. 15, 1889; Western Reserve University School of Medicine, Cleveland, 1917; service member of the American Medical Association; appointed an assistant surgeon in the medical corps of the U. S. Navy in June, 1917; his first duty assignment was at the U. S. Naval Hospital, Annapolis, Md.; during his more than 30 years of active service, served at Navy medical facilities throughout the United States and on board ships of the fleet; as senior medical officer of the USS Lexington, was awarded the Navy cross for his service in action against Japanese forces in the Coral sea on May 7 and 8, 1942; received the Purple Heart for wounds received in the same action; awarded the Victory Medal with Atlantic Fleet clasp, Marine Expeditionary Medal and the American Defense Service Medal with Fleet clasp; retired for reasons of physical disability on Jan. 1, 1947; recalled to active duty on Aug. 5, 1948; released from active duty on Feb. 28, 1950; died in the U. S. Naval Hospital, Annapolis, March 26, aged 67, of myocardial infarction with ventricular rupture.

Sumner, John Worthington, Jr., Lieut. Colonel, U. S. Army, Portland, Conn.; born in Lynn, Mass., Jan. 15, 1915; Columbia University College of Physicians and Surgeons, New York City, 1941; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War II; interned at the Central Islip (N. Y.) State Hospital and the Englewood (N. J.) Hospital; served a residency at the Walter Reed General Hospital (Army Medical Center) Washington, D. C., and Fitzsimons General Hospital in Denver, where he was chief of neurological section, neuropsychiatric service; served as chief of the neurological section, psychiatric and neurologic service, Brook Army Hospital; received the combat medical badge and Bronze Star; service member of the American Medical Association; died in Landstuhl, Germany, Feb. 24, aged 42.

Waggoner, Chester William ✦ Toledo, Ohio; born in Lindsey, Ohio, June 26, 1883; Toledo Medical College, 1906; specialist certified by the American Board of Internal Medicine; life member of the American College of Physicians; past-president of the Ohio State Medical Association and the Ohio State Medical Board of which he was a member for many years and at one time treasurer; member of the House of Delegates of the American Medical Association from 1927 to 1938; formerly health commissioner of Toledo; served on the staff of Maumee Valley Hospital and the St. Vincent's Hospital, where he died March 17, aged 73, of arteriosclerotic heaart disease and subdural hematoma.

Nicholson, Clarence M. ✦ St. Petersburg, Fla.; born in Kansas City, Mo., in 1868; Missouri Medical College, St. Louis, 1891; member of the Missouri State Medical Association; professor emeritus of surgery at St. Louis University School of Medicine; fellow of the American College of Surgeons; member of the House of Delegates of the American Medical Association in 1908; past-president of St. Louis Medical Society; served on the staffs of St. John's, St. Ann's, Mount St. Roses, Rebekah, and St. Louis City hospitals all in St. Louis; died in St. Antony's Hospital March 6, aged 89, of pyelonephritis and carcinoma of the urinary bladder.

Snow, Willard Groesbeck ✦ San Francisco; Harvard Medical School, Boston, 1939; assistant clinical professor of medicine at Stanford University School of Medicine; specialist certified by the American Board of Internal Medicine; a past-president of the Northern California Rheumatism Association and a director of the Northern California Chapter of the Arthritis and Rheumatism Foundation; veteran of World War II; chief of the arthritis clinic at Stanford University Hospital; on the courtesy staffs of St. Francis Memorial and Garden hospitals; died March 31, aged 43.

Tweedall, Daniel Greenwood ✦ Evansville, Ind.; born in 1881; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; member of the American Academy of General Practice; past-president of the Vanderburgh County Medical Society; medical examiner for Selective Service during World War I and II; on the staffs of Welborn Memorial Hospital, St. Mary's Hospital, and the Protestant Deaconess Hospital, where he served as staff president; died March 12, aged 76, of coronary infarction.

Reardon, William Francis, Hartford, Conn.; Baltimore Medical College, 1909; served three years as chairman of the Zoning Commission and one term as a member of the Board of Health; member of the Connecticut State Medical Society; twice president of the West Hartford Council; veteran of World War I; in July, 1925, was commissioned a captain in medical corps reserve; on the staff of St. Francis Hospital; died in the Veterans Home and Hospital, Rocky Hill, March 29, aged 70, of bronchopneumonia and carcinoma of the bladder.

O'Connor, Sylvester John ✦ Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1942; on the faculty at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the University Hospital and St. Joseph's Mercy Hospital; died March 10, aged 39, of coronary disease.

Alford, John Mosby, Oklahoma City, Okla.; Medical Department of Tulane University of Louisiana, New Orleans, 1895; an associate member of the American Medical Association; associate professor emeritus of medicine at the University of Oklahoma School of Medicine; died March 30, aged 85.

Allan, John Purcell, Lynchburg, Va.; Jefferson Medical College, Philadelphia, 1947; member of the South Carolina Medical Association; an associate member of the American Medical Association; resigned from the regular U. S. Navy on June 11, 1953; served as resident, Chesapeake and Ohio Hospital in Clifton Forge and the Lynchburg General Hospital; died April 8, aged 33.

Allen, Isaac Lathrop, Union City, N. J.; Long Island College Hospital, Brooklyn, 1903; veteran of World War I; formerly practiced in West Hoboken, where for many years he was school physician; died in the Christ Hospital, Jersey City, April 10, aged 75.

Allen, Leon Bernard ✦ Post Mills, Vt.; University of Vermont College of Medicine, Burlington, 1899; served as a member of the state legislature, and senator; assistant judge of Orange County Court; died March 19, aged 82, of myocardial infarction and arteriosclerosis.

Allison, Ira, Springfield, Mo.; St. Louis College of Physicians and Surgeons, 1903; served on the staff of the Burge Hospital; died in the Mercy Hospital April 12, aged 83, of arteriosclerosis.

Anderson, Stanley Charles ✦ Los Angeles; Rush Medical College, Chicago, 1929; member of the American Academy of Dermatology and Syphilology; served on the staffs of the Hospital of the Good Samaritan and the Children's Hospital; consultant for the Union Pacific Railroad and the University of California Student Health Center; died March 31, aged 57, of uremia, nephrosclerosis, and diabetes mellitus.

Ashby, Edward Clayton, Mount Airy, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1914; fellow of the American College of Surgeons; served four terms as city commissioner and two terms as mayor; veteran of World War I; on the staff of the Martin Memorial Hospital until his retirement; died in the Duke Hospital, Durham, March 7, aged 66.

Attwood, Archibald DeForest ✦ Denver; Gross Medical College, Denver, 1901; served on the staff of St. Anthony's Hospital, where he died Feb. 25, aged 87, of a cerebrovascular accident.

Babcock, Howell Edwards ✦ New York City; Jefferson Medical College of Philadelphia, 1915; veteran of World Wars I and II; died in the Forest Hills General Hospital April 6, aged 68, of cancer.

Barnard, Maurice Allyn ✦ Rochester, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1917; member of the American Academy of Occupational Medicine and the Industrial Medical Association; staff physician at Eastman Kodak Company's Kodak Park; on the staff of the Genesee Hospital; died April 12, aged 62, of heart disease.

Battaglia, Frederick Ignatius ✦ McKeesport, Pa.; St. Louis University School of Medicine, 1932; president of the entire medical staff and senior on the pediatric staff, McKeesport Hospital, where he died April 4, aged 49, of cerebral hemorrhage.

Baughman, Charles Benjamin, Elizabethton, Tenn.; University of Tennessee College of Medicine, Memphis, 1917; member of the Tennessee State Medical Association; fellow of the American College of Surgeons; veteran of World War I; member of the staff of St. Elizabeth General Hospital; died in Veterans Administration Center, Mountain Home, March 27, aged 62, of adenocarcinoma of the common bile duct with metastases.

Beckcom, Floyd Nash ✦ De Ridder, La.; Louisiana State University School of Medicine, New Orleans, 1941; member of the American Academy of General Practice and American Academy of Occupational Medicine; parish coroner; served during World War II; died in the Memorial Hospital, Lake Charles, March 26, aged 46.

Bekir, Nedjib Moustafa ✦ Philadelphia; University of Istanbul Medical Faculty, Turkey, 1918; member of the American Academy of Pediatrics; instructor in pediatrics at Jefferson Medical College; served as a captain in the Turkish Army during World War I; chief of pediatrics at Roxborough Memorial, St. Joseph's, and Nazareth hospitals; died in the Jefferson Hospital April 4, aged 62.

Belgrade, Joseph T. ✦ Wheeling, W. Va.; Jefferson Medical College of Philadelphia, 1919; member of the American Academy of Dermatology and Syphilology; on the staff of the Ohio Valley General Hospital; died April 8, aged 64, of acute myocardial infarction.

Benjamin, Harold Conrad ✦ Jersey City, N. J.; University and Bellevue Hospital Medical College, New York City, 1921; fellow of the International College of Surgeons and the American College of Surgeons; professor of orthopedics, Seton Hall University; staff member at the Fairmount and Christ hospitals, and the Jersey City Medical Center, where he died March 29, aged 58, of cerebral hemorrhage.

Besore, Albert Leroy, McClelland, Iowa; State University of Iowa College of Medicine, Iowa City, 1905; died Feb. 22, aged 77.

Bishoff, Mark Lincoln ✦ Topeka, Kan.; University Medical College of Kansas City, Mo., 1902; fellow of the American College of Surgeons; retired chief surgeon of the Atchison, Topeka and Santa Fe Hospital; spent two years on the medical staff of the Security Benefit Clinic and Hospital; died March 19, aged 89.

Bittner, Albert J., Allentown, Pa.; Boston University School of Medicine, 1893; served on the staff of the St. Luke's Hospital in Bethlehem; died in the Sacred Heart Hospital March 14, aged 87, of heart block.

Block, Alvin Phillips, New York City; Columbia University College of Physicians and Surgeons, New York City, 1909; on the staffs of the Lebanon Hospital and the Park East Hospital, where he died April 3, aged 69, of pulmonary embolism.

Bolognino, Octave Joseph ✱ San Francisco; Regia Università di Torino. Facoltà di Medicina e Chirurgia, Italy, 1914; member of the American Academy of General Practice; died in the Children's Hospital March 13, aged 69, of acute coronary occlusion.

Brandeberry, Nelson Albert ✱ Springfield, Ohio; Western Reserve University School of Medicine, Cleveland, 1930; veteran of World War II; on the staffs of the Mercy and City hospitals; died March 22, aged 54, of coronary occlusion.

Brown, Edward Augustus ✱ Indianapolis; Medical College of Indiana, Indianapolis, 1898; veteran of World War I; served on the faculty of his alma mater; died in St. Vincent's Hospital March 15, aged 84, of arteriosclerotic heart disease.

Brown, Wendell Phillips ✱ Lockland, Ohio; Eclectic Medical College, Cincinnati, 1912; member of the American Academy of General Practice; served on the staffs of the Bethesda, Christ, and Good Samaritan hospitals in Cincinnati; died March 21, aged 74, of arteriosclerotic heart disease.

Burnette, Elmer Wiggins, Tarpon Springs, Fla.; Atlanta Medical College, 1915; served on the staff of the Tarpon Springs Hospital; died March 9, aged 67, of heart disease.

Cansler, Hurnon Kirk, Temple, Texas; Marion-Sims College of Medicine, St. Louis, 1894; died March 14, aged 99.

Carman, Paul Irvine, Cincinnati; University of Minnesota Medical School, Minneapolis, 1915; died March 25, aged 67, of coronary embolism.

Caudle, Gardner Robert, Greenville, S. C.; North Carolina Medical College, Charlotte, N. C., 1910; died March 12, aged 70, of coronary thrombosis and hypertension.

Champlin, Howard William ✱ Chicago; University of Illinois College of Medicine, Chicago, 1920; senior staff member of the Ravenswood Hospital, where he died April 8, aged 73, of gastric ulcer with hemorrhage.

Chappelle, William D. Jr., Columbia, S. C.; Leonard Medical School, Raleigh, N. C., 1913; died March 6, aged 68.

Craddock, Azzore Willard, St. Louis; Meharry Medical College, Nashville, Tenn., 1902; died March 19, aged 85, of cancer.

Daniele, Francescantonio Michele, North Hollywood, Calif.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1905; served in the medical corps of the Italian Army during World War I; died March 21, aged 77, of coronary thrombosis.

Dawson, Francis Phillip Jr. ✱ Waltham, Mass.; Tufts College Medical School, Boston, 1931; assistant in medicine at Harvard Medical School; formerly on the faculty of his alma mater; past-president of the Massachusetts Trudeau Society; member of the American Trudeau Society; superintendent of the Middlesex County Sanatorium; died March 13, aged 50, of coronary arteriosclerosis.

De Niord, Richard Newnham ✱ Buffalo; University of Buffalo School of Medicine, 1915; served on the faculty of his alma mater; fellow of the American College of Physicians; member of the Endocrine Society; veteran of World War I; on the staffs of the Millard Fillmore Hospital and the Buffalo General Hospital, where he died March 22, aged 68, of adenocarcinoma of the colon.

Gourley, Eugene Vincent ✱ Detroit; Wayne University College of Medicine, Detroit, 1939; fellow of the American College of Surgeons; veteran of World War II; associated with the Mount Carmel Mercy Hospital, where he died March 8, aged 44.

Graf, John Edward ✱ Morton Grove, Ill.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1905; member of the Indiana State Medical Association; veteran of World War I; died April 11, aged 83, of arteriosclerotic heart disease.

Herlong, Mark Boyd, Starke, Fla.; Medical College of South Carolina, Charleston, 1908; died Jan. 19, aged 81, of cholangioma.

Hess, Valentine Martin ✱ Washington, D. C.; Temple University School of Medicine, Philadelphia, 1925; fellow of the International College of Surgeons and the American College of Surgeons; served on the faculty of the Georgetown University School of Medicine; member of the staff of the Providence Hospital, where he died March 16, aged 59, of acute coronary occlusion.

Hood, Addie Clark, Cicero, Ill.; Jenner Medical College, Chicago, 1901; died March 26, aged 84, of cerebral vascular accident.

Hudson, Jessie Blanche ✱ Hampton, Iowa; State University of Iowa College of Medicine, Iowa City, 1908; died Dec. 22, aged 86, of heart disease.

Hunter, Alfred Lewis, Pax, W. Va.; University of Louisville (Ky.) Medical Department, 1909; served as a member of the Fayette County Board of Education; died March 31, aged 75, following a heart attack.

Ketcham, Mary Emma Coffin, North Miami, Fla.; Cleveland Homeopathic Medical College, 1905; died in Daytona Beach March 18, aged 84.

Koch, John Christian ✱ Detroit; Johns Hopkins University School of Medicine, Baltimore, 1917; died March 16, aged 75, of coronary thrombosis.

Kramer, Richard Shaffer, Jennings, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1919; member of the Louisiana State Medical Society; served as school board member; on the staff of the Jennings American Legion Hospital; honorary member and past-president of the Jennings Rotary Club; died Feb. 6, aged 63, of carcinoma of the larynx.

Kriechbaum, Horace Theodore, Davenport, Iowa; Northwestern University Medical School, Chicago, 1908; served on the staffs of the Mercy Hospital and St. Luke's Hospital, where he died March 19, aged 72, of lobar pneumonia and acute myocardial infarction.

Land, William Alonzo ✱ De Kalb, Miss.; Memphis (Tenn.) Hospital Medical College, 1901; died March 19, aged 83, of bronchopneumonia.

Larsen, John Bertram ♦ Morris, Ill.; Rush Medical College, Chicago, 1932; member of the American Academy of General Practice; served as a member of the board of education; on the staffs of St. Joseph's Hospital in Joliet and the Morris Hospital; a member of the Chamber of Commerce; died March 18, aged 63, of cancer.

Lazelle, Horace Gibbs, San Diego, Calif.; University College of Medicine, Richmond, 1900; an associate member of the American Medical Association; formerly police surgeon for La Jolla; veteran of World War I; served on the staff of Scripps Memorial Hospital in La Jolla; died in Hillcrest Manor, National City, March 19, aged 86.

Leonard, Carroll Francis ♦ East St. Louis, Ill.; St. Louis University School of Medicine, 1931; senior instructor in internal medicine at St. Louis University School of Medicine; chairman of St. Clair County Tuberculosis Association; associate physician, St. Mary's Group of Hospitals; on the staff of the Christian Welfare Hospital; director of the East Side Public Health District; died in St. Mary's Hospital March 19, aged 52.

Levin, Samuel Orrin ♦ Denison, Texas; University of Illinois College of Medicine, Chicago, 1934; served on the staff of the Madonna Hospital; died April 6, aged 48.

McClendon, Henry L. ♦ Palestine, Ark.; University of the South Medical Department, Sewanee, Tenn., 1899; veteran of World War I; past-president of St. Francis County Medical Society; died Feb. 17, aged 82.

McCrann, Patrick Michael ♦ Rock Springs, Wyo.; John A. Creighton Medical College, Omaha, 1918; veteran of World War I; county health officer; member of the American Academy of General Practice; died Feb. 4, aged 62.

McInturff, David Nathaniel Jr. ♦ Lieut. (jg) U. S. Navy, retired, Sunnyvale, Calif.; University of Oregon Medical School, Portland, 1930; entered the U. S. Navy on June 26, 1930, and retired June 30, 1937; veteran of World War II; served on the staffs of the San Jose (Calif.) Hospital and the Palo Alto (Calif.) Hospital; died Feb. 14, aged 54, of carcinoma of the lung.

MacLean-Kennedy, Clyde, Port Chester, N. Y.; University of Western Ontario Faculty of Medicine, London, Ontario, Canada, 1924; veteran of World War I; on the staff of the United Hospital; member of the Medical Society of the State of New York; died Feb. 5, aged 63, of acute myocardial insufficiency.

McPherson, Samuel Preston, Chewelah, Wash.; Homeopathic Medical College of Missouri, St. Louis, 1898; formerly councilman and mayor of Chewelah; died in Santa Maria, Calif., Feb. 10, aged 87.

Maher, Ruth Antoinette, Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1952; interned at the Grant Hospital; an Army nurse during World War II; died Feb. 22, aged 46.

Marino, Joseph, Valley Stream, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1925; died Dec. 17, aged 61, of a heart attack.

Marvel, Philip Jr., Atlantic City, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1917; past-president of the Atlantic County Heart Association; veteran of World War I; died Feb. 23, aged 64, of acute coronary thrombosis.

Mederos, Luis Orlando ♦ Augusta, Ga.; Universidad de la Habana Facultad de Medicina y Farmacia, Cuba, 1942; specialist certified by the American Board of Psychiatry and Neurology; member of the Illinois State Medical Society; on duty with the U. S. Army; died March 15, aged 39, in an automobile accident.

Merchant, Raymond, Lake Village, Ind.; Rush Medical College, Chicago, 1932; on the courtesy staff of the Methodist Hospital in Gary; since 1945 on the staff of the U. S. Steel Mills in Gary, where he died Feb. 9, aged 54, of coronary thrombosis.

Miller, Olga Alice, Ukiah, Calif.; University of California School of Medicine, San Francisco, 1929; past-president of the Mendocino and Lake Counties Medical Society; served on the staffs of the Mendocino State Hospital in Talmadge and the Atascadero (Calif.) State Hospital; died in San Francisco March 1, aged 53, of cardiac arrest during surgery.

Mills, Jamison Cottrell, Toledo, Ohio; Meharry Medical College, Nashville, Tenn., 1916; died in the Mercy Hospital March 8, aged 64, of bronchogenic carcinoma.

Monosmith, Olney B., Lorain, Ohio; College of Physicians and Surgeons of Chicago, 1893; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the honorary staff of St. Joseph Hospital, where he died March 8, aged 85, of myelogenous leukemia.

Montgomery, Colonel Harry ♦ Los Angeles; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1902; M. R. C. S., England, and L. R. C. P., London, 1907; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; died March 19, aged 80.

Montgomery, Robert Clinton ♦ King, Wis.; the Hahnemann Medical College and Hospital, Chicago, 1894; veteran of World War I; died Feb. 25, aged 85.

Mulligan, Ralph Mitchell ♦ Reading, Pa.; Medical College of Virginia, Richmond, 1934; fellow of the American Academy of Allergy and member of the American College of Allergists; interned and served a residency at St. Joseph's Hospital, where he was chief of medicine and in 1952 he was named staff president; died Feb. 25, aged 52, of injuries received in an automobile accident.

Munster, James A., Pittsburgh; Maryland Medical College, Baltimore, 1912; an associate member of the American Medical Association; assistant staff member,

South Side Hospital, where he died Feb. 23, aged 75, of arteriosclerotic heart disease, nephrosclerosis, and pneumonia.

Musa, Agha Buzurkhan, West Hartford, Conn.; Jefferson Medical College of Philadelphia, 1916; specialist certified by the American Board of Psychiatry and Neurology; service member of the American Medical Association; member of the American Psychiatric Association; for many years associated with the Veterans Administration; served during World War II; died in the Hartford (Conn.) Hospital Feb. 13, aged 67.

Myers, Eugene Lee ✱ St. Louis; St. Louis College of Physicians and Surgeons, 1909; assistant professor of otolaryngology at St. Louis University School of Medicine; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; member of the consulting staff at Jewish Hospital, where he died March 12, aged 73, of dissecting aneurysm of the aorta.

Nadeau, Alexandre T. ✱ Marinette, Wis.; Rush Medical College, Chicago, 1902; fellow of the American College of Surgeons; past-president of the Marinette County Medical Society; died in St. Joseph Lloyd Hospital in Menominee, Mich., March 3, aged 79.

Neal, Harry Beecher ✱ Indiana, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1906; served on the Indiana Borough School Board and board of health; for many years treasurer of the Indiana County Medical Society, of which he was president, vice-president, and secretary; died Feb. 25, aged 74, of acute coronary occlusion.

Nenner, George, New York City; New York Homeopathic Medical College and Hospital, New York City, 1927; member of the Medical Society of the State of New York; for many years associated with the New York City Health Department; district health officer in charge of the Tremont District Health Center; veteran of World War II; died in the Montefiore Hospital March 25, aged 52.

Nissen, Harry Archibald ✱ Sherborn, Mass.; Harvard Medical School, Boston, 1916; specialist certified by the American Board of Internal Medicine; served on the faculty of his alma mater; associated with the Palmer Memorial, New England Deaconess, and Robert Breck Brigham hospitals in Boston; died Dec. 14, aged 65, of coronary occlusion.

Nix, Milton Arthur ✱ Princeton, Ill.; Northwestern University Medical School, Chicago, 1910; past-president of the Bureau County Medical Society and the North Central Medical Society; veteran of World War I; past-president of the Perry Memorial Hospital staff; died April 4, aged 74, of pneumonia.

Norwood, Ballard Jr., Oxford, N. C.; Medical College of Virginia, Richmond, 1937; past-president of the North Carolina Public Health Association; served as health officer of Granville County; died March 5, aged 45.

Seitz, Charles Lewis, Evansville, Ind.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; served as vice-president of the Welborn-Walker Hospital, now known as the Welborn Memorial Baptist Hospital; surgeon on two polar expeditions; founder and director of the Evansville Radium Institute; died Feb. 23, aged 79, of arteriosclerosis.

Tretbar, Friedrich Wilhelm ✱ Stafford, Kan.; Kansas City (Mo.) Medical College, 1905; served on the board of education; a charter member and first president of the Stafford Lions Club; died in the Stafford Hospital March 18, aged 76, of cerebral sclerosis.

Vinje, Syver, Hillsboro, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; member of the North Dakota State Medical Association; formerly city health officer, state senator, and member of the city commission and school board; died Feb. 14, aged 87, of arteriosclerosis.

Wallace, Clifton Robert, Winston–Salem, N. C.; George Washington University School of Medicine, Washington, D. C., 1907; formerly associated with the U. S. Public Health Service and the Veterans Administration; during World War II served as medical director of the National Bureau of Standards, U. S. Department of Commerce, in Washington, D. C.; died March 23, aged 73, of arteriosclerotic heart disease.

Warren, Roy Chester, Yukon, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1928; also a graduate in pharmacy; veteran of World War I; served as a member of the board of regents at his alma mater; died Feb. 12, aged 57, of chronic emphysema.

Whitlock, William Albert, Pendleton, S. C.; University of Georgia Medical Department, Augusta, 1901; died in the Anderson (S. C.) County Memorial Hospital Feb. 24, aged 90, of lobar pneumonia.

Whitney, Lawrence Luther, Welch, W. Va.; George Washington University School of Medicine, Washington, D. C., 1905; located in McDowell County in 1914 and served as physician for several coal companies; on the staff of the Welch Emergency Hospital until his retirement in June, 1956; died in Bluefield March 19, aged 76, of coronary failure.

Wilcox, Guy S., Ada, Ohio; Toledo Medical College, 1900; veteran of World War I; on the staffs of the San Antonio Hospital and Hardin Memorial Hospital in Kenton, where he died Feb. 15, aged 86, of a fracture of the hip and arteriosclerosis.

Wilson, Mille E., Plainwell, Mich.; Michigan College of Medicine and Surgery, Detroit, 1903; a member of the staff of the Lapeer (Mich.) State Home and Training School for 41 years prior to her retirement in 1948; died March 15, aged 80.

Witmeyer, Harry Calvin, Lebanon, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1900; served as city councilman; died in the Good Samaritan Hospital Feb. 1, aged 82.

Wood, Neill B., Steens, Miss.; University of Virginia Department of Medicine, Charlottesville, 1901; died March 9, aged 80.

FOREIGN LETTERS

AUSTRIA

Repository Penicillin.—At the meeting of the Vienna Society of Physicians, on March 29, Doujak and Hueber said that penicillin preparations with lower solubility were being elaborated to prolong absorption. Their absorption rate was compared, with the aid of blood-level determinations, with the duration of their retention in the body. Therapeutically effective blood levels were maintained for about 24 hours with the usual doses of procaine penicillin G with a solubility of 0.4%. Benzathine penicillin G with a solubility of 0.014% and penicillin V with a solubility of 0.034% were compared with procaine penicillin G. It was shown that benzathine penicillin G produces longer lasting levels in the body, whereas penicillin V, which produces higher initial blood levels, is more rapidly eliminated. Sufficient therapeutic levels can be maintained safely for more than 72 hours with a dose of 600,000 units of benzathine penicillin G and 800,000 units of penicillin V. To obtain greater therapeutic safety, it was suggested that the blood level be increased by using benzathine penicillin G with additional doses of alkaline penicillin alone or combined with procaine penicillin G or with additional doses of penicillin given by mouth.

The median blood levels produced with the use of procaine penicillin G averaged 6.57 units per cubic centimeter after 2 hr., 0.345 units per cubic centimeter after 24 hours, 0.329 units per cubic centimeter after 48 hours, and 0.177 units per cubic centimeter after 72 hours. When the blood levels were raised by giving 120 mg. of penicillin every four hours by mouth and simultaneously giving additional intramuscular doses of penicillin V, the initial levels were 1.5 units per cubic centimeter whereas values of about 1.06 units per cubic centimeter were observed after 72 hours. No side-effects were observed. Local pain was noted in the area of the injection after 10 to 20% of the injections, but this did not necessitate withdrawal of the drug.

Treatment of Pancreatitis with Cortisone.—At the same meeting, A. Fritsch said that, although the results of treatment of acute pancreatitis have improved, they are still unsatisfactory. Evaluations of new method of treatment of this disease are difficult. At the Kaiser Franz Joseph Hospital eight patients with hemorrhagic pancreatitis have been treated with cortisone since November, 1956; seven were cured; one died. Diagnosis was established in seven patients by laparotomy. Hydrocortisone was injected locally around the pancreas during operation on three patients. Postoperative recovery was uneventful despite the severity of the lesions.

Osteomyelitis.—At the same meeting, F. Endler stated that the local focus of osteomyelitis cannot always be completely cured, although general therapy with large doses of antibiotics as well as local treatment of abscess cavities are used in treating acute osteomyelitis. Extensive radical operation is necessary in treating chronic osteomyelitis, in addition to the giving of antibiotics. The speaker reported on a series of 215 patients with acute, and primarily chronic, osteomyelitis. The principle of the treatment is the transcutaneous, hermetically closed instillation of the drug through a waterproof steel cannula inserted into the bone. The diffusion and course of absorption in the diseased bone could be clearly followed up roentgenographically with the aid of a contrast medium. The drugs applied were selected according to the susceptibility of the infectious bacteria and instilled daily for two to five weeks. Satisfactory results were obtained in 38 (95%) of 40 patients with primary disease, whereas in 139 (86.9%) of 160 patients with chronic osteomyelitis a continuous inactive state could be obtained. Many of these patients who had severe inoperable conditions with progressive amyloidosis have been cured by this method.

Vectorcardiography in Infants.—At the meeting of the Vienna Pediatric Society, held in March, Wenger and Hupka reported that, in a series of 22 newborn infants, vectorcardiograms were recorded 30 minutes after birth and later at regular intervals. The vectorcardiograms of 18 infants taken a few hours after birth showed a marked preponderance of the right side of the heart that disappeared after several days. It was hypothetically assumed that, after the closure of the foramen ovale, an increase of the minute volume of the right ventricle occurred, associated with a temporary physiological overloading of this ventricle. When the resistance in the lesser circulation decreased, an adjustment and partial restoration to normal occurred in the electrocardiographic or vectorcardiographic findings. Analogous findings occur in cases of acute cor pulmonale. The principal emphasis must be laid on the closure of the foramen ovale during the hemodynamic changes that are responsible for the described changes of the vectorcardiogram. Even if the foramen ovale should close soon after birth, an overloading of the right ventricle might be apparent from the vectorcardiogram only a few hours after birth.

Causes of Death in Nursing Infants.—At the same meeting, H. Orel stated that 0.51% of nursing infants died of congenital malformations in 1956, about the same percentage (0.43%) as in 1935. Death during delivery was recorded more frequently (0.85%) in 1956 than (0.56%) in 1935, perhaps due to the fact that 21 years ago there were fewer autopsies of infants than at present. The most frequent causes of death are

---

The items in these letters are contributed by regular correspondents in the various foreign countries.

still prematurity and multiple birth (1.78% in 1956 compared with 2.8% in 1935). The diagnosis "defective vitality of babies carried to full term" is rarely made in Vienna. The death rates due to bronchitis and bronchopneumonia (0.51% in 1956 compared with 1.4% in 1935), to gastroenteritis or dystrophy (0.57% in 1956 compared with 0.7% in 1935), and to other diseases (0.3% in 1956 compared with 1.91% in 1935) show a decrease. This decrease is not satisfactory if compared with the corresponding figures for the northern and western countries of Europe, because these deaths are due to diseases that could have been prevented. Vienna appears to have a higher death rate than West Berlin due to erythroblastosis (0.08% compared with 0.01%) and during delivery (0.86% compared with 0.28%) but a lower rate due to premature or multiple births and defective vitality (1.73% compared with 2.18%). In Vienna the death rate within the first week of life amounted to more than twice than that in Holland in 1955 (2.63% compared with 1.19%). The rate of stillbirths was low in Vienna, amounting to 1.6% in 1956. The speaker explained the relatively high death rate of infants (4.6%) in Vienna, a city with a birth deficiency (the birth rate was 0.81%), where 97% of all deliveries take place in lying-in hospitals, as due to induction of labor by puncture of the membrane, lack of will to raise children, and occupation of mother outside the home. Therefore the speaker was skeptical of the prospects for improvement of results by intensifying the care of pregnant women and nursing infants in Vienna.

Poliomyelitis Vaccine.—At the same meeting, W. Auerswald discussed the recent concepts with regard to the safety and efficiency of trivalent poliomyelitis vaccine inactivated with formaldehyde. It appeared that freedom from infectious virus is not guaranteed by retrospective tests of tissue cultures but by the careful regulation of the process of inactivation on the basis of objective important points for the decrease of activity during the action of formaldehyde on the virus suspension. Additional safety is obtained by filtration of the inactivated virus suspension through filters with extra fine pores. The neutralization test, by inoculation into the spinal marrow of a monkey treated with cortisone, might reveal aggregates of virus. The examination of effectiveness in animal experiments is not entirely satisfactory, especially because of the impossibility of preserving a standard of potency. The epidemiologic evaluation of the results of vaccination in 1956 shows that, although the instructions for vaccination had not been strictly observed, about 75% of the paralytic forms had been prevented. The prophylactic effect against the nonparalytic form of the disease was less favorable. Only a few allergic side-effects of the vaccination were observed. In only an occasional vaccinated person was there a relation between vaccination and a subsequent attack of poliomyelitis. Examinations of persons who were vaccinated at the culmination point of the disease at an epidemic center offered no proof of a provocative effect of the vaccination.

BRAZIL

Potassium Metabolism.—Dr. Alberto Benchimol (*O Hospital* **52**:253, 1957) reported on the clinical and electrocardiographic disturbances of potassium metabolism in 17 patients. All the patients but one were female, and their ages varied from 10 to 58 years (average 40). Each patient had been given one of the following diagnoses: (1) lower nephron nephrosis and diabetes; (2) obstructive jaundice, stenosis of the common bile duct, and acute necrosis of the renal tubules; (3) lower nephron nephrosis and retroperitoneal fibrosarcoma; (4 and 5) diabetic acidosis; (6) subacute glomerulonephritis with renal insufficiency; (7) chronic glomerulonephritis with renal insufficiency; (8) carcinomatous obstruction of the sigmoid; (9) ulcerative colitis; (10) choledocholithiasis, choledochostomy, and hypotonic dehydration; (11) duodenal ulcer and gastrectomy; (12) posthepatic cirrhosis, hepatic insufficiency, and metabolic acidosis; (13) subacute glomerulonephritis; (14) hepatosplenic and intestinal schistosomiasis, splenectomy, and pulmonary embolism; (15) hepatosplenic and intestinal schistosomiasis; (16) diarrhea of unknown cause; and (17) low serum potassium level of unknown cause. A low serum potassium level was present in 11 of the patients. An electrocardiogram was taken of 13 patients. The other four all had a low serum potassium level. The most frequent abnormalities shown by the 13 electrocardiograms were the flattening and inversion of the T wave, found in 7 patients, and a prolonged QT interval, found in 4. In three of the seven patients presenting marked electrocardiographic changes, the potassium level in the blood serum was normal. The author believes that the lowered serum potassium level was not the only cause of the electrocardiographic changes in some of the patients but that there were also electrolytic alterations, such as lowered sodium, calcium, and bicarbonate levels. Basing his opinion on the study of these patients, he believes there is no direct and constant correlation between the electrocardiographic changes and the serum potassium level.

Control of Leprosy.—At a meeting of the São Paulo Academy of Medicine, Dr. L. M. Bechelli, of the São Paulo State University, said that, when the division of leprosy was created in the state department of health in 1922, the leprosary was considered the most important weapon against the disease, the dispensary being rated as having only a limited influence. All recognized lepers, whether they had the lepromatous or the tuberculoid form of the disease, were confined to a leprosary. Discharges were granted only after 24 months of negative examinations. This routine has been completely changed by modern treatment. The discovery of the lepromin reaction made it possible to determine the state of immunity of the patients, to forecast the favorable or unfavorable course of the disease, and to furnish a basis for controlling the contacts. The positive reactors (20%) should receive special care, while the negative reactors are already im-

mune. A better knowledge of the indeterminate and tuberculoid types of leprosy indicates that both are benign forms that do not need isolation and can be treated in dispensaries. The sulfones control the incipient forms of the disease and often improve the patients with lepromatous leprosy to the point that they can be discharged from the leprosary. The use of BCG vaccine appears to increase the patient's resistance to Mycobacteria in general. Today, the leprologist is able to discover the disease in its early stages, thus permitting treatment at a time when the disease can be aborted. These advances have made the dispensary the principal place of treatment for the disease. The chief functions of the leprosy dispensary, of which there are about 50 in the state of São Paulo with more than 10 million population, are early diagnosis, early treatment, control of contacts, health education, follow-up of patients discharged from leprosaries, selective isolation, and control of fugitives from leprosaries. At present, there is one case of leprosy per 400 inhabitants in the state of São Paulo.

CANADA

Civil Defense.—In December, 1952, the Canadian Medical Association collaborated with the Department of National Health and Welfare of the federal government in publishing a special issue of the *Canadian Medical Association Journal*, containing material on civil defense. A second symposium on this subject appeared in a March issue of the same journal under the same auspices. Dr. Charron states that 13 cities have been named as potential enemy targets. These jointly contain an aggregate population of over 5,800,000 people, or about 33% of the entire population of Canada. Civil defense planners consider that the major challenge is the rapid movement of populations of this magnitude and the reception of these persons in smaller communities. Planning for civil defense is based on the following phases: (1) preattack evacuation of certain large cities in which the population will be thinned out by evacuating priority groups such as children, the aged, expectant mothers, adult disabled, and ill; (2) planned withdrawal from certain cities to be put in operation on the alert signal; (3) action after the incident in attack areas; and (4) aid and rehabilitation, involving both disaster cities and reception areas. Dr. Charron emphasizes the need for the coordination of health services and the other civil defense services and for a close working relationship with the United States. He points out that about 50% of the hospital beds in Canada are situated in target areas. New units will have to be established in reception areas. Medical and public health laboratories will have to be relocated, as will blood banks, which are now mostly in vulnerable areas. Dr. Charron divides the health services into medical services, public health, special weapons, and medical supplies.

A reappraisal of the civil defense health services program has been under way for the past two years. The basic principles established for defense against the smaller bomb are still considered practical for defense against the larger weapon. They consist of (1) peripheral mobilization of personnel and transportation supplies, (2) central deployment of civil defense forces to the area of devastation, and (3) mobile support from communities outside the disaster area. Some services have undergone changes after the reappraisal. The primary treatment services required to operate advanced treatment centers, giving first aid and primary treatment, as close to the disaster site as possible have been halved in size, with stress on flexibility and mobility. Increasing emphasis has been given to improvised hospitals which are mobile and can be transported in one large trailer or four 3-ton trucks. These can be set up in two or three hours, either as an extension of an existing hospital or as a separate unit. They will be used mainly in reception areas. Planning for hospital evacuation from cities has been greatly facilitated by a time-motion study that demonstrated that a 500-bed hospital could be evacuated in four or five hours. By decentralizing blood banks, it is hoped to establish a service capable of collecting about 300,000 pt. in 72 hours.

Great importance is attached to emergency public health arrangements in disaster areas and reception communities. The main problems will be control of infectious disease and provision of adequate sanitation. Here original plans have had to be modified to allow for changes due to radioactive fall-out. The medical supplies program has been expanded to allow for care of casualties and noncasualties in self-contained improvised hospitals. Most of the basic plans have been completed and are now in the stage of implementation. The concept accepted in Canada is that civil defense health services should be developed now to the degree necessary for peacetime emergency and that these units should form the nuclei around which major wartime services could be built. Although over 800 primary treatment service units will be needed for Canada as a whole, the present planning allows for about 400 to be established after consultation with the provinces. Nucleus units will provide a scaled-down version of the war establishment with all essential component parts. Operation equipment is being stockpiled and training units are available.

The hospital program is well advanced and has been developed by a series of regional hospital disaster institutes that have been attended by representatives of over 250 hospitals. Over 400 physicians have attended courses on the medical aspects of disaster planning at the Canadian Civil Defense College. Short courses of training for undergraduate medical students have been approved in principle. Altogether, 35,000 Canadian nurses have received some instruction in civil defense, and eight provinces have established courses of training for undergraduate nurses. Pharmacists and dentists have also been included. Canadian planners have pioneered in the field of casualty simulation, and a textbook is now available from the federal government.

Orders have been placed for about 67% of the supplies originally listed as essential to civil defense needs. Most of this material will be delivered in the next fiscal year. The department of national defense is act-

ing as storing agency for these supplies, and regional depots are being established across the country in less vulnerable areas so that supplies will be readily available for any potential target. The main depots will be under federal supervision, but when a state of emergency occurs supplies will be distributed to points under provincial and local control. Progress made in developing civil defense health service plans at provincial and local level has been variable. Some provinces have achieved little. At the moment, emphasis is shifting from central planning to provincial and local implementation.

In another article, Brigadier Crawford describes the organization and function of primary treatment services for civil defense. These consist of a casualty collecting unit and an advance treatment center. The function of the casualty collecting unit is purely one of first aid and transportation and does not include the use of physicians or nurses. The advance treatment center is the first point in the chain of evacuation at which the casualty can receive any professional medical care. It is, however, primarily an evacuation unit, and any medical or surgical procedure undertaken there is intended to save life or to support the patient during his removal to hospital. A number of locations outside target areas have already been designated as assembly points for primary treatment services.

Health Services for Civil Servants.—The civil service health division of the Department of National Health and Welfare of Canada was established in 1945. Its first facilities were ready for operation in April, 1947. It has now published a monograph in which development and progress in health service during a 10-year period are reviewed. This service was charged, in the first place, with the responsibility for providing a health service program for civil servants and other federal government employees. Terms of reference were broad, comprising prevention and control of disease, accident prevention, emergency treatment, supervision of working conditions, health education, and advice to departments and individuals.

The federal government employs about 150,000 persons, distributed from coast to coast, including about 135,000 civil servants and 15,000 employees of crown companies and corporations. The largest concentration, about 34,000, is located in Ottawa. Observers over the past nine years have suggested that government workers are more likely to be affected by mental and emotional illness than are those in industrial plants and factories, whereas injuries on duty and diseases resulting from exposure to occupational hazards are less common. The civil service health division contains a health center that combines administrative headquarters and clinical facilities in Ottawa and a number of health units staffed by nursing counselors on a scale of one for every 500 to 700 employes. The division provides a basic advisory service to all government departments, reviewing and analyzing medical certificates of disability, making statistical health studies on morbidity, starting a program of health education, reviewing medical examination reports on personnel starting or changing jobs, and making special examinations when necessary. The health center with its staff of physicians, including a psychiatrist, a psychologist, a part-time radiologist, a social-welfare supervisor, and public-health nurses, provides a diagnostic and advisory service to about 32,000 government employees in Ottawa. Their first responsibility was to investigate and, where necessary, physically examine employees referred from health units, with special reference to suitability for certain employments, and to give routine immunizations. Treatment at the health center was restricted to emergency medical and surgical care of minor conditions. Any greater defect was referred to the patient's family physician.

The health units were in the charge of well-qualified, full-time nursing counselors. Employees were encouraged to visit these on return to work. The nursing counselors were regarded as case-finders, who would at all times have available to them medical advice and complete facilities for medical investigation of problem cases at the health center. The case load has become increasingly heavy. The psychiatrist has had a double role, that of sponsoring a mental health program by education and that of helping nursing counselors to detect early psychiatric difficulties. The average monthly number of health-unit visits per 100 personnel supervised started at 33, rose to 75 after five years, and has now dropped back to 58. Evaluation of the work of nursing counselors suggested that over 70% of visits to them after casual absence and 80% after certified absence were of definite value. The counselors believed that over 80% of all casual absences and 90% of all certified absences were justifiable. This suggests a fairly large margin of abuse of the liberal sick leave given in the federal service. About 97% of the employees who visited the nursing counselor were returned to work after medical care or consultation with the health unit. It is noted that the civil service feels morally obligated to employ a much higher percentage of veteran and civilian handicapped than does private industry. Continued employment of many of these persons is only possible through the availability of nursing, counseling, and health-unit facilities. Employees with serious heart conditions, diabetes, epilepsy, war disabilities, and other conditions are thus enabled to increase their span of usefulness by many years.

Drinking and Driving.—The province of Saskatchewan has passed a Consolidated Vehicles Act that contains a new and controversial item. As of April 1, it became compulsory for motorists holding a Saskatchewan license to take a drunkometer or "breathalizer" test if requested by the police. If a driver is stopped on suspicion of being under the influence of alcohol and refuses to submit to a breath test, his license may be suspended for up to 90 days, provided that the licensing board is satisfied that mental or physical disability has prevented ordinary control over the vehicle, that there is lack of skill in handling the vehicle, or that the subject's driving habits or conduct are dangerous. As originally drafted the law was even more stringent,

and the government at first required blood, saliva, and urine tests, in addition to the breath test. They also wished legislation to allow for indefinite suspension of a license. As the law now stands the traffic board will have to have a hearing, after 90 days, in the presence of the license holder before it can further suspend or revoke the license. There are three difficulties in the way of implementing this act. 1. It is contended that drunken and impaired driving are criminal code offenses and that the province lacks authority to undertake tests for alcohol. This feature was found unconstitutional in New York state. 2. There are those who contend that breath analysis is not sufficiently reliable for measurement of competency of a driver. 3. The difficulty will arise of not having sufficient trained personnel and equipment available for all police departments in the province to undertake testing when necessary.

DENMARK

Prevention of Deafness.—Recent legislation enables every Dane, irrespective of his age and fortune, to seek free advice concerning difficulties over hearing at any of the three state hearing centers. The center in Copenhagen began work in 1951, and in the subsequent five years it dealt with 13,356 persons. An analysis of these cases by Dr. H. W. Ewertsen in *Nordisk medicin* for Jan. 31, 1957, shows that 54.8% of this number were over the age of 65, whereas only 9.4% of the population of Denmark is over this age. The services of this center have been so greatly appreciated that about 42% of all the older persons who are hard of hearing have been treated there. On the other hand, this was the case with only 16% of the persons who were hard of hearing in the wage-earning age groups. About 60% of the patients suffered from ailments of the inner ear, such as senile involvement of the nervous system. The remaining 40% suffered from faulty conduction of sound due to such ailments as chronic adhesive or perforating otitis media and otosclerosis. The new law (1955) obliges the employer to take the necessary precautions against accidents, including injuries to the ears. He must pay for medical examinations, and the worker must submit to them.

Treatment for Gallstones.—At a meeting of the Danish Surgical Society, Dr. F. Truelsen reviewed the experiences of the Odense County Hospital during the period 1940 to 1955. During that period victims of gallstones have been admitted to the hospital in growing numbers, at a higher average age, and with a much lower operative mortality. The number of patients admitted yearly has risen from about 80 to 400, and the number of operations yearly from about 50 to 200. During the period 1940 to 1943 the operative mortality was 7.5%. It fell to 1.8% in the period 1952 to 1955. Between these periods the operative mortality for women under the age of 44 years fell from 3.4% to none. For women between the ages of 55 and 64 years it fell from 9.7% to 0.7%. For men under the age of 65 it fell from 15.7% to 0.9%. After the age of 65 it was over 10% for both men and women. At the beginning of the period under review the maximum incidence occurred in patients in the age group 35 to 55 years, whereas in the latter part of the same period the maximum had shifted to the age group 45 to 65 years. The per cent of patients over the age of 65 rose in the same period from 14 to 20.

Treatment of Cholecystitis.—At the same meeting and drawing their material from the same hospital, Drs. K. Kristensen and S. Lyndrup gave an account of the 272 patients with cholecystitis treated during the period 1945 to 1950. Nearly all the 213 patients discharged from the hospital with intact gallbladders were reexamined in 1955, only 14 patients having died or not having been traced. In 44% the patients were either well or had died of causes other than cholecystitis. Another 24% were moderately well, and 31% were ailing or had been operated on after discharge. From this survey it was concluded that (1) cholecystitis is an indication for immediate admission to the hospital; (2) if conservative treatment is advised, it should be rigidly adhered to; and (3) a previous severe attack of cholecystitis should be an indication for an operation in the absence of special contraindications.

Lethal Poisons on the Farm.—The growing use of various chemicals in farming has its inevitable sequel of fatal poisonings. In *Ugeskrift for læger* for Feb. 28, 1957, Prof. Poul Bonnevie gives an account of the 69 deaths that occurred in Denmark during the seven-year period 1949 to 1955 as the result of poisoning with various chemicals. His list of 30 different chemicals includes lead (five deaths), gasoline (six deaths), methanol (one death), and nicotine (5 deaths). Since the adoption in 1954 of a law concerning poisons used by the farmer, there is some hope of stricter control of them, and Bonnevie urges the householder to be more circumspect with the family medicine chest and such commonly used chemicals as acids and alkalis. In the same seven-year period there were 318 deaths from various drugs other than so-called technical poisons used on farms; 216 of these were due to soporifics. Morphine accounted for 59 and various other drugs for 43 deaths. It has been calculated that more than 1% of the population is admitted to the hospital every year, about 50,000 for traumatic lesions and about 5,000 for acute poisoning. About 3,000 of this number represent suicidal attempts (successful and unsuccessful) and about 1,000 acute alcohol poisoning.

INDIA

Detection of Ovulation.—P. N. Wahi and co-workers have studied the relation between vaginal cytology and sterility. A comparative study of serial smears, endometrial biopsy specimens, and estimation of urinary pregnanediol was undertaken to determine any correlation between the vaginal smears and progesterone activity. Patients with inflammatory diseases of the uterine cervix, corpus, and adnexa were excluded by careful examination before the smears were

taken, as pathological discharges profoundly alter the vaginal smear. During the course of the study, douching, coitus, and endocrine and intravaginal medication, all of which alter the vaginal smear, were forbidden. The serial vaginal smear findings of 48 women were correlated with the endometrial biopsy specimens only and of 40 other women with both endometrial biopsy specimens and estimation of urinary pregnanediol. The ovulatory menstrual cycle was characterized by a smear pattern that consisted of menstrual, postmenstrual or early follicular, late follicular, ovulatory, and premenstrual phases. The curling of cells or desquamation and grouping accompanied by a decline in the number of cornified cells were observed in the cases in which endometrial biopsy specimens showed that the secretory phase and urinary pregnanediol were present. These findings with fully cornified cells showing evidence of maximum desquamation can be regarded as evidence of ovulation. Smears varying widely from the above pattern are suggestive of ovulatory failure. The disorder of patients with such smear findings was considered histologically to be proliferative, and in women with such smears pregnanediol was absent from the urine. In both groups one phase was almost always followed by the next. The ovulatory phase, when clearly present, was seen from the 14th to the 26th day in a regular cycle of 28 to 30 days. Hence there is a possibility that the nature of the cycle may be diagnosed by a single smear study during the premenstrual phase (24th to 26th day) in a normal cycle of 28 to 30 days. The study thus suggests that vaginal smears can help in the diagnosis of the presence or absence of ovulation.

Vaginal Cytology in Liver Dysfunction.—Sachdev and Sachdev (*Indian Journal of Medical Sciences,* February, 1957) state that the vaginal and cervical epithelium is sensitive to the influences of certain hormones, particularly the estrogens. Normal estrogen metabolism depends on a healthy state of the liver. Decreased inactivation of estrogens during liver disorders has been reported in human beings by some researchers. The present investigation was undertaken to study the effect of liver damage on estrogen metabolism as reflected in the vaginal cytology; 480 vaginal smears obtained serially from 41 patients with hepatic cirrhosis and infectious hepatitis were studied. The authors tried to correlate the cytological findings with the clinical findings and the findings of the liver function tests. Vaginal smears were found to have a limited application in the assessment of the extent of liver damage. The authors suggest that estrogen metabolism is disturbed probably late in these liver disorders. On the basis of clinical observations, they imply that adrenal dysfunction is probably a forerunner of disorders of estrogen metabolism.

Rauwolfia Alkaloids.—M. Sirsi and co-workers (*Indian Medical Record,* November, 1956) state that crude total alkaloids of Rauwolfia possess both central depressant and peripheral adrenolytic action. Hypothermia, diminished metabolism, drowsiness, and the autonomic imbalance noticed after prolonged administration of these alkaloids suggest the loci of action to be in the hypothalamus. A close relationship exists between the autonomic nervous system and genital functions. Since the hypothalamus is one of the integrating centers for the autonomic functions, drugs that either cause autonomic imbalance or hypothalamic depression are likely to interfere with the normal physiology of the gonads. Since crude total alkaloids depress the hypothalamus and cause autonomic imbalance by adrenolytic action, the influence of this drug on ovarian function was studied and compared with that of reserpine. Reserpine given daily intraperitoneally in a dose of 20 mcg. per kilogram of body weight for a period of 14 days produced a slight functional disturbance of the ovaries, as seen by the interference with the cyclic changes of the estrus in rats. The effect of 0.2 mcg. of crude total alkaloids per kilogram of body weight given for the same duration was more severe. Besides functional derangement, reduction in the weight of the ovaries was noticed. An attempt to make clear the locus of action for these endocrine disturbances by studying the variations in the estrus cycle and weight changes of ovaries under different experimental conditions has revealed that neither the vaginal epithelium nor the functional capacity of the ovary is deranged by crude total alkaloids and that the observed changes are due to a diminished reactivity of the pituitary in its gonadotropic hormone secretion.

Scholarship for Study of Tuberculosis.—The National Association for the Prevention of Tuberculosis, London, has offered a scholarship in the amount of $980 to a medical graduate from India for the study of tuberculosis in the United Kingdom. The candidate will be selected by the Tuberculosis Association of India and will be expected to work with tuberculous patients in India after the training. The program will include two months' study of different forms of collapse therapy, pathology, administration, records, and sanatorium routine; one month of specialist training according to the orthopedic, genitourinary, or thoracic interest of the candidate; one month's study in the treatment of tuberculous children, diseases of bones and joints, and tuberculous meningitis; six weeks' study of domiciliary treatment, follow-up of contacts, tuberculin testing, BCG vaccination, aftercare, and rehabilitation; and two weeks' study of miniature and large x-ray films, darkroom technique, records, organization, and radiologic equipment.

SWEDEN

Doctors on Strike.—The conflict between the Swedish medical profession and the municipal authorities of several important towns is but one aspect of a larger problem involving, on the one hand, the academic and professional classes and, on the other, state and municipal authorities. Architects, lawyers, librarians, and other professional workers have joined together in a body known as the Central Swedish Academic

Organization. The Swedish Medical Association is one of several bodies affiliated with this organization. In recent years all the members of the learned professions have felt the pinch of salaries kept fixed while the cost of living has soared. While private employers have met rising costs with rising wages, the state and, still more so, the municipal authorities have delayed in making the adjustments necessitated by rising prices. In the autumn of 1956, the central government revised the remuneration for its employees, but the municipal authorities were slow to take their cue in this respect. At the Sahlgrenska Hospital in Gothenburg, matters came to a head with the withdrawal of many physicians from their hospital appointments after due notice had been given. Arrangements were made for consultations and treatment to be given outside the hospital, and a private surgical clinic has been treating several hundred patients daily. The skeleton hospital staff still on duty sees to it that the public is not victimized, while at the same time patients not in urgent need of hospitalization are referred to private practitioners. The Gothenburg strike began on April 8 and has spread to Stockholm and Malmö. Several hundred members of the medical staffs of the municipal hospitals in Stockholm have handed in their resignations to take effect on June 15.

Recent Advances in Thoracic Surgery.—Dr. P. Rudström (*Svenska läkartidningen*, April 5, 1957) states that the number of nontuberculous patients undergoing lung operations rose from 5 in 1949 to 50 in 1956. In the same period there was a rise from 99 to 120 in the number of patients undergoing lung operations for tuberculosis. The number of patients undergoing cardiac operations rose from 4 in 1953 (the first year in which such operations were performed) to 57 in 1956. There was also a marked rise in the number of patients undergoing operations on the esophagus, stomach, and diaphragm. Most of the patients undergoing a thoracic operation for some nontuberculous disease suffered from cancer. As thoracotomy only hastens the end in inoperable cases, Rudström has learned to appreciate greatly the value of a supraclavicular lymph node biopsy. This test of operability has now become a routine measure in patients suspected of having lung cancer. Of a series of 1,280 patients undergoing some sort of thoracic operation, 896 did so on account of pulmonary tuberculosis. Lobectomy has grown in popularity (a rise from 8 such operations in 1949 to 59 in 1956), and thoracoplasty has fallen in popularity (64 such operations in 1949 and 17 in 1956). Extrapleural pneumothorax or open pulmolysis has been practically abandoned.

Vertigo.—Vertigo is apt to bring its victims into many different types of hospital wards, as is attested to by the fact that, of the 178 patients reported on after an otoneurological follow-up examination, 82 had been treated in a medical department, 82 in an ear department, and 14 in a surgical or gynecologic department of a general hospital. Dr. N. Wastenson (*Svenska läkartidningen*, March 8, 1957) classified these 178 patients according to the diseases responsible for the vertigo. To simplify matters, he allotted only one cause of the vertigo to each case, although it was not always easy to distinguish between a combination of causes in individual cases. Labyrinthine hydrops (Meniere's syndrome) was the cause in 37 cases, cerebrovascular disease in 30, psychic insufficiency in 22, postencephalitis in 12, damage to the labyrinth in 12, intoxications in 10, tumor in 8, and a host of such other ailments as cardiovascular disease and migraine in smaller numbers of cases. In 12 cases, no diagnostic label could be attached. Of the 30 patients suffering from cerebrovascular disease, 27 had been over 50 years of age when the vertigo had set in. On the other hand, most of the 22 patients suffering from psychic insufficiency were under 50 years of age. Three of the 10 patients whose vertigo was of toxic origin had been treated with streptomycin. Wastenson pleads for teamwork in which physicians, psychiatrists, and otologists cooperate to discover the causes of veritgo. When some somatic cause of vertigo is not obvious, there must be a lookout for some psychic cause, and the otologist can be most useful in eliminating or clinching a purely otological diagnosis. In 28% of Wastenson's patients, some peripheral, vestibular cause of the vertigo was found, and it is this class of patient that should be under the care of an otologist.

Misuse of Corticosteroids.—From the skin department of the Caroline Hospital in Stockholm comes a warning by Drs. Gentele and Lodin against the use of corticosteroids or corticotropin in the treatment of psoriasis, which is so common in Sweden that its frequency has been put at from about 0.1% to 1.5% of the population. They admit that knowledge of this disease has not grown appreciably in the past 50 years and that there is not yet any effective internal treatment. External treatment is also far from ideal. In their series of 12 patients, treatment with corticosteroids was disappointing, and they have yet to learn of a single patient in whom this treatment has been successful.

UNITED KINGDOM

Social Service Debate.—The government has been criticized by the socialist party for its attitude on social services. In a debate, on March 19th, Dr. Edith Summerskill attacked the government's recent decision to reduce the food subsidies, to increase the price of school meals and milk and also welfare milk, and to increase charges for prescriptions. She thought that this revealed a disregard of the needs of the poorest. The Minister of Health, Mr. Dennis Vosper, maintained that, in establishing the policy, it was recognized that the amount which could be spent on the social services is not unlimited and that it is important to eliminate waste and inefficiency and to insure the availability of services to those most in need. He pointed out that it is now possible to allocate 56 million dollars to hospital building and he hopes this can be increased. Better recruitment to hospital staffs has resulted in better use of hospital beds so that the number of those on waiting lists has fallen from 526,

000 in 1953 to 433,000 in 1956. In the past five years, 2,000 more general practitioners joined the service, and the number of dentists now practicing is the highest ever known, even though still not enough. The exchequer was bearing 80.2% of the total cost of the health service, and the recent increase in contributions would reduce this figure to 74.1%, at the same time insuring that those who were employed would help pay the expenses of those who were not, although most of the cost would still be borne by the taxpayer.

Sir Spencer Summers said that there was a danger that the ever-growing cost of social services might, if uncontrolled, destroy the whole system. He suggested that it would be reasonable to expect people to carry individually the normal running expenses of life, such as glasses, and a normal family of two children. Hazards of old age or a serious operation should be safeguarded by the community. If the present family allowance for the second child in wage-earning families were discontinued, then a further 160 million dollars would be available for other useful purposes, such as pensions. Mr. R. P. Hornby pointed out that the percentage of the cost of the health service borne by public funds is greater in Great Britain than in any other country in Europe. The figure for Belgium is 32%, in Sweden and Denmark 30%, and in Norway about 22%. The question of the free treatment of foreign visitors was also raised, particularly in view of the recent refusal to increase the pay scale for physicians, and the necessity to increase weekly subscriptions. Although the total cost of such treatment has been only about $160,000, informal steps have been taken to refuse entry into the country of persons suspected of arriving simply for free expensive operations or other facilities. The expense of closing this loophole would probably amount to more than the present cost. Naturally emergency treatment is available to all visitors.

Gastric Emptying Rate.—Dr. J. N. Hunt and co-workers at Guy's Hospital, London, investigated the emptying rate of the stomach in a series of young men and women. The gastric emptying rate depends on the normal propulsive power and the inhibitory mechanisms stimulated from the duodenum by contact with gastric contents. The test meals used consisted of (1) a saline solution containing 100 mEq. per liter of sodium chloride and (2) distilled water. The difference in emptying rate after ingestion of the two gave measure of the effectiveness of the duodenal braking action. The authors concluded that the propulsive powers of the stomach and the effectiveness of the duodenal inhibitory mechanisms were equal in the two sexes and not altered in the presence of a duodenal ulcer. It was, however, confirmed that the acidity of the gastric contents was higher in men than in women after a test meal, presumably due to a higher secretory response. The secretion of acid, chloride, and pepsin was about 1.5 times as great in the men. The authors concluded that this might be a significant factor in causing duodenal ulcers but that differences in the rate of gastric emptying played no part at all.

The Gastroesophageal Sphincter.—The nature of the closing mechanism between the stomach and esophagus is still a matter of dispute. Mr. G. S. M. Botha, formerly lecturer in surgery at Birmingham University, with his co-workers further investigated this problem. His subjects were adult volunteers, mainly medical students. Others were those who had had the exact site of the esophageal hiatus marked at laparotomy by a wire clip. The use of esophageal tubes of polythene, 2.5 mm. in diameter, and with a balloon end enabled manometric recordings to be made. Pressures were recorded as the tube was withdrawn from the stomach into the esophagus, and the course of a radiopaque marker in the end of the tube was recorded by cineroentgenography. In other cases, no balloon, but just an open-end esophageal tube, was used. A series of 227 gastroesophageal withdrawal pressure curves were obtained, 133 being recorded on the open tube system and 94 on the balloon system. A combined cineroentgenographic localization was effected in 129 cases. The authors concluded that a mechanism operates in the lower segment of the esophagus and produces a compressing effect for a distance of 0.5 to 5.6 cm. This may vary, in any one subject, both in extent of pressure changes and location. The variable pressure seemed unrelated to the "crural pinchcock" mechanism, since it was not always greatest at inspiration. In the normal subject, probably the most important component of gastroesophageal closure is the intrinsic sphincteric mechanism, but other factors, no doubt, play a part.

Umbilical Granuloma.—Granuloma of the umbilicus in infants is not uncommon, but, whereas the part played by talc in the pathogenesis of granulomatous lesions within the abdomen and elsewhere has been clearly established, there were no published reports of its relationship to umbilical lesions until Creery and co-workers (*Lancet*, March 30, 1957) reported five such cases. The umbilicus typically showed a pink granulomatous mass of tissue discharging a purulent exudate. Histological examination revealed doubly refractile talc particles frequently associated with a foreign-body giant-cell reaction. It would appear that talcum powder, in these cases, delayed healing by creating conditions favorable to persistence of infection. The authors suggest that such powders should not be used until the umbilicus is completely healed, since the powder is no substitute for proper cleansing and thorough drying. In view of the firmly rooted practice of using such powders, however, the authors believe that, unless umbilical granulomas from this source become more prevalent, the practice is likely to continue.

Defective Poliomyelitis Vaccine.—The Ministry of Health announced, in a letter of March 11 concerning 47 defective vials in the latest batch of poliomyelitis vaccine, that contamination by Pseudomonas fluorescens had occurred due to faulty containers. Repeated sterility tests on the remainder of the batch have been negative, and tests by incubation at various temperatures have caused no discoloration of the normally

colored vaccine. In agreement with the Medical Research Council, it was decided, therefore, to issue the rest of this batch of vaccine for use.

Happiness and Marriage.—In a television program on March 21, a statistical report was given on the results of a questionnaire answered by 6,000 women. It was carefully pointed out that the group was not truly representative of the country. It was found that 71% of the women considered themselves very happily married, 23% fairly happy, and 6% unhappy. Factors contributing to a happy marriage were a satisfactory physical and sexual relationship, mutual confidence, the wife not working outside the home, a happy childhood, and the freshness of the marriage. Apparently after 20 years of marriage the number of those in the very happy group fell from 85 to 62%. An acquaintanceship of several years before marriage appeared to be an advantage. The wife who accepted her husband with his bad habits and was not intent on changing him usually had a happy marriage. Money had little influence on the happiness of the marriage. Too many children had a negative effect, although this effect might also be attributed to the length of the marriage. Only 3% of the women sought a husband with good looks; 56% thought that life was easier for men; and 34% of the happily married thought it possible, after marriage, to fall in love with someone else. Nevertheless, 76% said they would marry the same man again. Such an analysis, although not of statistical significance, is of interest to the general practitioner often confronted with the marital problems of his patients.

Pay Increases for Junior Hospital Staff.—All hospital authorities have received instructions from the Ministry of Health to increase by 10%, after April 1, the salaries of hospital medical and dental staff up to the grade of senior resident. The new rates of pay per annum (with old rates in parentheses) are $3,388 ($3,080) rising to $4,312 ($3,920) after four years for senior residents, $2,618 ($2,380) in the first year and $2,972 ($2,702) in the second or subsequent year for residents, $2,387 ($2,170) rising to $3,311 ($3,010) for junior interns, and $1,309 ($1,190) to $1,618 ($1,471) for senior interns.

Blood Fatty Acids in Coronary Disease.—The observation that atheromatous plaques are predominately lipid in composition has encouraged many attempts to correlate the incidence of corronary-artery disease with abnormalities of lipid metabolism and with an excessive fat intake. James and co-workers, using the recently developed technique of gas chromatography, which has made possible the direct isolation, identification, and analysis of all the fatty acids between C_6 and C_{20} from a few milligrams of fatty acids, have examined the latter in the blood of 12 patients with coronary-artery disease (*Lancet* 1:705, 1957). The blood of 12 normal subjects of the same age and sex was examined for comparison. Dietary histories, including the daily intake of fat and calories, were taken from both groups. For purposes of analysis, the blood was divided into red-blood-cell, plasma-phospholipid, and plasma-acetone-soluble fractions. In the red-blood-cell and plasma-phospholipid fractions there were no detectable differences between the amounts of fatty acids in the blood of persons in the two groups. In all three fractions the average amounts of the essential fatty acids (linoleic and arachidonic) were about the same in the patients and in the controls. The observations of James and his co-workers thus do not support the view put forward by Sinclair that deficiency of these fatty acids is a factor in the genesis of coronary-artery disease. In the acetone-soluble fraction of the plasma there was an indication of an increase in the combined amounts of monosaturated C_{14}, C_{16}, and C_{18} acids in the blood of the patients compared with the controls. The ratio of the most abundant of these acids (oleic) to its corresponding saturated acid (stearic) was higher in the patients with coronary-artery disease.

Leeds Bone Bank.—A bone bank has been established in Leeds General Infirmary, a teaching hospital of Leeds University. Bone, mainly from the lower end of the femur and the upper end of the tibia, is taken from volunteers up to 30 years of age. Most of the bone, which is cancellous, is reduced to chips, but some is cut into narrow strips. The bone is placed in sterile tubes and processed in a simple apparatus in the department of bacteriology. Sterilization is done with a 1% solution of beta-propiolactone in isotonic saline solution at 37 C for two hours. The sterilized contents of the tube are drained free of fluid, tested for sterility, and freeze-dried. At operation the bone is used in its dried state, reconstitution occurring in the tissues of the recipient. So far, 80 patients have been supplied with bone from the bank. Such bone is easily stored, does not require thawing before use, and being friable can easily be packed into cavities. Before freeze-drying, such bone can be cut to sizes ready for use.

Failure of Penicillin to Prevent Leptospirosis.—Although penicillin is effective in the treatment of leptospirosis in man, Broom and Norris state that it is of no protective value if given prophylactically at the time of infection with the spirochete (*Lancet* 1:721, 1957). A laboratory worker, handling cultures from one of the Leptospira javanica serogroups, dropped a syringe containing a live culture on his foot, the needle penetrating the skin and subcutaneous tissues. Penicillin was given immediately and repeated every six hours, until a total dose of 6,000,000 units had been given. The wound healed but on the 8th day became red and sore, and on the 10th day the patient had the clinical signs of leptospirosis. He was given 250 mg. of oxytetracycline every six hours for five days, after which his general condition improved. At the height of his illness leptospirae were isolated from his blood, which also contained agglutinins for the particular strain.

Collective Neurosis.—Prof. V. Frankl of the Neurological Polyclinic in Vienna, in an address before the Austrian Institute in London in February, said that during the years he had been in concentration camps

he had had ample opportunity to observe both himself and others under conditions of stress. Neuroses have by no means increased in frequency in the decade after World War II, but the symptoms have changed. Anxiety has decreased in prominence. Quantitatively, psychotherapy has increased, and today some patients who would be more suited to visit a priest go to a psychiatrist. Clinical neurosis has by no means become collective, and what might be called "collective neurosis" is not necessarily a neurosis. Symptoms akin to collective neurosis fall into categories of ephemeralism, fatalism, collective thinking, and fanaticism. The first two are widespread in the western world, probably as a sequel to the war when men lived from day to day. They will probably increase with the boredom of the average worker as his leisure is increased in the machine age. In collective thinking the individual desires to be inconspicuous, preferring to be submerged in the mass. Finally, the fanatic denies the personality of others while, in actual fact, he has no personality of his own.

Venous Thrombosis.—In the *British Medical Journal* of March 16, Dr. Witold Rudowski states that he produced thrombosis experimentally in dogs. After he had injected a 50% solution of sodium salicylate into a dog's vein, thrombosis appeared in 6 to 12 hours, and organization was first seen after seven days. If 200 mg. of heparin sodium is given daily, beginning 6 to 24 hours after the production of thrombosis, further development of the thrombus is prevented. If started after three days, it exerts no influence. The application of procaine paravertebral block less than six hours after the production of the thrombus prevents its full development, but this treatment must be continued for at least four days. These opinions were based on histopathological examinations only and need to be supplemented by an analysis of phlebographic appearances for the evaluation of dynamic changes of blood supply in these lesions.

Compensation for Pneumoconiosis?—In 1929 a man became a moulder in a firm of ironfounders. His job was the filling of moulds with molten metal and then knocking out the forms. In this process clouds of dust and sand were emitted. The man's health deteriorated. In 1946 he was seriously affected, and in 1954 he was largely incapacitated by silicosis. As a result of a claim of negligence against his employers for not providing a respirator, he was awarded $27,000 damages. On appeal, the court directed a new trial on the question of whether failure to provide a respirator was a breach of the employer's obligation under the Factories Act and, if so, to what extent it had contributed to the claimant's condition. Until about 1950 it had not been recognized by any competent person that the ordinary work of a foundry moulder could cause pneumoconiosis. At that time there was only one efficient respirator available capable of providing protection against silicosis. It was pointed out that precautions taken had to be in the light of established knowledge and that it was not known at the time the worker contracted the disease that it could happen as a result of this employment. No one denied that the disease had been contracted from the particular form of employment, but as there had been no willful breach of duty and therefore no negligence by the employers at that time the decision was reversed.

Prison Reform.—Overcrowding is a serious problem in the prisons. This is being met by new construction, but, more important, it is being met by reducing the inflow of prisoners, especially those with short sentences. Forms of treatment are provided for certain offenders, and reform schools are used to keep young people out of prisons and to provide a focus for research into juvenile delinquency. Prisons are still understaffed, but the emphasis is on recruiting the right kind of men and women for this work. Pay and conditions of service are being reviewed, but the home secretary stressed the vocational aspects of this occupation. At Norwich prison, an experiment in which new prisoners were assigned to small groups, each having its own two officers, has been successful, and an improved prisoner-staff relationship has resulted. More attention must be given to raising the self-respect of prisoners and training them to accept their family and social responsibilities. This could well be done by allowing the prisoner to earn full wages out of which he could support himself and his family and even compensate his victim, thus working out his own personal redemption. Under such conditions a prison may no longer be just a simple place of punishment but an institution where an offender repays his or her debt not only to the society whose order he has disturbed but to the fellow members of that society whom he has wronged.

University Funds.—The universities of Great Britain face financial difficulties, a fact that is recognized by the government and reflected in the recent increase announced in the treasury grants. At present such grants provide 72.7% of the universities' income compared with 66.5% provided in 1951-1952. The universities' disinclination to become entirely dependent on the state, either for maintenance or capital expenditure, fosters their habit of self-help and economy and is one of the reasons for their reluctant decision to raise their fees to students. The increase in fees starts in the 1957-1958 school year and will bring in additional revenue of about $1,500,000. In spite of 87 million dollars spent on building in nine years, the needs have by no means been met. Overcrowding still exists in libraries, lecture rooms, and dining halls, and some laboratories and scientific research departments are housed in primitive quarters. Twice as many pupils remain in school till the age of 17 years as was the case in 1939, and the increase in university scholarships from public funds has increased the number of students enrolled to a total of 88,701—the highest ever. The distribution of students among the colleges is now shifting, science and technology gaining at the expense of arts and medicine; 2,441 students began their medical course in October, 1956, compared with 2,614 in 1953. The total number of medical students in the country is 13,035, or 14.7% of all students, compared to 23.8% in the 1938-1939 school year.

CORRESPONDENCE

EFFECTS OF DETERGENTS ON SKIN CONDITIONS

To the Editor:—I read with interest Dr. R. R. Suskind's recent report (THE JOURNAL, March 16, page 943) on the effects of detergents on skin conditions. I object to Suskind's conclusion that detergents are not capable of causing skin damage, as well as the logic involved in basing such a conclusion on the experiments cited in the report. It is an everyday clinical fact that women engaged in household work do suffer from hand dermatitis much more frequently than do those in other occupations in which frequent contact with surface-active cleansing agents does not occur. Time and again, these patients report aggravation of their eruptions after contact with cleansing agents, and there is visible evidence of such reaction in the erythema, edema, and even vesiculation which result. It has been impossible in these clinical cases to effect a cure without strictly prohibiting contact with soap and synthetic detergents.

Why do the experiments reported by Suskind fail to demonstrate the known inflammatory reactions attributable to some surface-active agents? Experiments carried out and reported by myself (THE JOURNAL, March 13, 1954, page 894) and others have shown that it is possible to produce dermatitis by repeated hand soaking in detergent solutions. The concentration and temperature of the detergent bath and the frequency of exposure and its duration are important factors in determining the number of reactions in these studies. Females are more susceptible than males, and the winter months render subjects much more reactive to the irritating effects of detergent soaking. As with any irritant, by varying the concentration one can change the number which will show reactions. The concentrations which I have found will cause inflammation in the majority of subjects are somewhat above those used by Suskind. The subjects employed have normal skins but are not hospitalized and are allowed to expose their hands as usual in their daily work.

Discrepancies between Suskind's results and those of other workers can therefore be explained on the basis of these quantitative variations in experimental conditions. The question is, which conditions are closer to real life usage? It appears reasonable to me to carry out these tests in the wintertime, when most cases of "housewive's eczema" are seen, to use female subjects, and to employ the concentration of detergent present in the foam in dishwater. This concentration is sometimes substantially higher than the 0.5% used in the detergent bath by Suskind. Under such conditions, exposure to the detergent referred to by Suskind will produce inflammation of the skin in a higher percentage of subjects. The dermatitis produced experimentally is morphologically similar to ordinary "dishpan hands." If one accepts Suskind's data as given, one must reach a conclusion which experience demonstrates is entirely unacceptable: that aqueous solutions of a highly alkaline, phosphate-containing "heavy duty" detergent not only are nonirritating but are actually beneficial in cases of eczematous dermatitis.

MATTHEW J. BRUNNER, M.D.
1400 Otto Blvd.
Chicago Heights, Ill.

The above letter was referred to the author of the article, who replied in part as follows:

To the Editor:—One essential condition of the study was to determine, if possible, the effect on the skin of the detergent or soap product alone. We attempted to reduce the patients' cutaneous exposure factor to 1 by removing them from their household or occupational milieu and hospitalizing them for two to three weeks, during which time the detergent or soap solutions were essentially the only materials to which their hands were exposed.

During the first week of the test one hand was immersed for 30 minutes twice daily in 0.5% solution of a synthetic detergent washing product at 105 F and during the second week in the same concentration of the soap washing product. The sequence of these immersions was alternated in each subject. The control hand was immersed in tap water at 105 F for the same period as the test exposure. The tests were carried out both in winter and in summer, but the environmental conditions in the hospital were, of necessity, relatively constant. Before we started these immersion studies we suspected that the dermatitis of the test hands of our subjects would become worse when exposed to the detergent solutions under the test conditions. Contrary to our expectations, we observed that, under the conditions of the immersion, both the test and the control hands of the majority of patients improved. The pattern of response of the control hand was uniformly identical with that of the test hand. In other words, when improvement or deterioration was observed in one hand, it was also observed in the other. One cannot conclude from this observation that the detergent immersion is therapeutic, as Dr. Brunner has. The improvement, as I have stated in the paper, "may be attributed either to the anti-inflammatory effect of the soaking or to the hospitalization itself, which removes the patient from the milieu responsible for the eruption." In some instances no improvement was shown, but, contrary to our expectations, in no instance did we observe that the test hand became worse by comparison to the hand exposed to the tap water only. The reasonable interpretation to be given is that dermatitis of the hands (including eczematous dermatoses) is not made worse by isolated, repeated immersion of the hand in solutions of at least two household washing products under conditions of concentration, temperature, and duration comparable to that of usage.

Since this paper was read in June, 1956, the number of subjects under study has doubled. We have also altered the frequency of immersion to six times per

day, keeping the temperature of 105 F and total duration of 60 minutes constant. The pattern of results remains the same.

How does one explain the apparent difference between the response of our subjects to washing product exposures in the hospitals and that of the housewife or houseworker in the working milieu? Although the exposure conditions of the average housewife with regard to concentration and duration are somewhat less severe than those of our subjects, many other factors may play an active part in common usage exposure which were not present in the hospital exposure, e. g., the components of dish and laundry soilage, food dyes, meat, fruit, vegetable juices, metals, solvents as in polishes or cleansers, fabrics, ambient temperature and humidity (winter environment is a known potent factor), mechanical trauma, bacterial or fungal infection, and even the tension and stress of the social environment. In the usage exposure about which we are so concerned clinically, there is an interplay of these diverse factors which include soap and detergent immersion.

Nowhere in my report is there any statement which Dr. Brunner attributes to me "that detergents are not capable of causing skin damage." What I have said (page 945), and I believe my recent observations substantiate this, is that "it appears that the circumstances that cause soap or detergent dermatitis include the cleansing agent as one of a set of complex factors." Dr. Brunner believes that we failed to demonstrate cutaneous injury because of the concentration and temperature of our solution. There is no doubt, too, that detergents or soaps in much higher concentrations and higher temperatures such as Dr. Brunner employed in his own published experiments will damage the normal or diseased skin. However, the conditions of his exposures under which irritation was produced are rarely, if ever, encountered in household usage conditions. In order to determine, with some degree of accuracy, usage conditions for the average housewife, we carefully surveyed a group of 180 housewives for a seven-day period and found that the average concentration of dish and laundry soap or detergent solutions and the average daily exposure were even lower than our experimental conditions. Repeated immersion of the hand in 2 to 4% concentrations of the anionic detergent employed by Dr. Brunner is irritating. It is only fair to point out, however, that these concentrations are 7 to 14 times greater than that employed in average household use. The temperature of his immersion solution, 138.6 F, is not only much higher than usage but one which most women would find it impossible to tolerate for more than a very few minutes, and patients with hand dermatitis would not tolerate at all. Although Dr. Brunner's experimental conditions induced irritation, they were obviously much more severe than those that are encountered in usage. In any appraisal of biological hazard, appreciation of the degree of exposure to a given material encountered under usage conditions is of primary importance. It is only in the light of such quantitative considerations that one can interpret the significance of experimental results.

I would agree with Dr. Brunner that, under household and occupational conditions, dishwashing and laundering may provoke or aggravate eczematous hand dermatitis despite the fact that the detergent employed may not be specifically indicted in experimental exposures. I would certainly agree with him that one cannot effect a cure in most instances without prohibiting immersion of the hands in dish and laundry water, as well as restricting soap and water cleansing. These clinical observations do not contradict those made experimentally. They simply indicate that the provoking exposure is not limited to a single injurious agent but includes a set of factors which will induce damage when they are operating simultaneously.

Raymond R. Suskind, M.D.
The Kettering Laboratory
University of Cincinnati College of Medicine
Cincinnati 10.

LIABILITY OF PHYSICIANS

To the Editor:—I wish to express a few opinions concerning the current series of articles in the section Medicine and the Law. On the whole the topics are well chosen and presented. To date Mr. Morris' article on *res ipsa loquitur* (The Journal, March 23, page 1055) is one of the clearest explanations of this problem available in any medical periodical. It is extremely difficult indeed to translate complicated legal theory into understandable lay terms. Mr. Morris has succeeded. His scope is complete, thorough, and pointed. The arguments are well founded. His advisement of better medical cooperation is especially well taken, for this is certainly one positive way to counter the courts' reasons for applying such a "rule of sympathy."

Generally the doctrine of *res ipsa loquitur* is fair to both doctor and patient when the facts of the particular case properly raise an inference of negligence. Yet, since it is a judge-made rule, it can be restricted and extended almost at will depending upon the dictates of the socioeconomic environment of the period. All the court need do is to find some substantial policy consideration upon which to rest its hat. With the growing tendency toward guaranteed individual security and welfare as evidenced by the actions of both legislatures and courts, the struggle to preserve pure legal theory is rapidly fading. In many respects this trend cannot be condemned, for in a population the size of ours there are circumstances where the interest of society as a unit must outweigh individual consideration. It has been argued that this same policy must take precedence over the physicians' interests, i. e., there must be compensation for all untoward results of medical procedures, whether negligently caused or not. This is the underlying rationale for the "rule of sympathy," in effect a device whereby the physician is required to pay regardless of proof of fault, based on an improper inference.

Throughout the cases setting forth this rule there is no doubt that the courts are following social patterns to decide the controversy. However, they are doing so by indirect means. Instead of being forthright, declaring that physicians' liability will be determined not by

fault but by economic pressures, the courts are compelled by precedent to remold existing legal principles to achieve the desired result. This is the state of affairs in California. *Res ipsa loquitur* is being applied to raise an inference of negligence in cases where such an inference is not justified in the first instance. This practice should be attacked in the strongest possible terms. Whenever a physician has caused an injury through his negligence, the judgment for compensation is expected. On the other hand, when he is held accountable for an injury not because he was at fault but because he was unable to extricate himself from an improperly imposed inference, then he has been unjustly harmed. No one relishes being sued, least of all when the deck is stacked. This is particularly true of a physician since his professional and personal reputation is a matter of public concern. It is probable that quite a few procedures plagued with a calculated risk will be hesitantly used, if at all, to prevent exposure to such liability. This is human nature and will be a definite deterrent to full realization of the proposed Principles of Medical Ethics as published in the April 13th issue of THE JOURNAL, page 1364 [especially Section 6: "A physician should not dispose of his services under terms or conditions which (1) interfere with or impair the free and complete exercise of his independent medical judgment and skill . . ."]. Perhaps even more important is where the particular procedure proves to be of invaluable aid in diagnosis or treatment. The public then loses more in medical benefits than it gains in economic compensation. It would be far better to say openly that physicians are to be held liable regardless of fault than to create a fiction of negligence upon which to award damages to the injured.

I have attempted to emphasize these points in a recent comment (30 *South. California Law Rev.* 80-88) with particular reference to the California decisions. In all fairness, it is to be noted that California virtually stands alone in this extension of the "rule of sympathy." However, although the Pennsylvania Supreme Court in a recent case [*Robinson* v. *Wirts*, 127 A. (2d) 706] refused to apply *res ipsa* in a calculated risk situation, the opinion was accompanied by a vigorous dissent. There is little doubt that the trend throughout the country is to ease the requirements of an injured person to maintain a cause of action against physicians. California has taken the lead—others may follow.

DON H. MILLS, M.D.
School of Law
University of Southern California
3518 University Ave.
Los Angeles 7.

MEDICAL MISSIONARY WORK

To the Editor:—As everyone knows, medical work in mission lands is of great importance, as many of these countries are so far behind our own remarkable development in this regard. Many millions are without any hope of profiting by the marvelous advances of modern medicine, unless new means are developed to aid them.

One very promising enterprise in this direction is the establishment of the new community, the Sons of Mary, Health of the Sick, at Sylva Maria, Framingham, Mass. The purpose of this community is new. So far as we know, it is the only one of its kind in the world.

Its first objective will be to establish educational centers in the most favorably located districts in mission lands, where there is a sufficient number of educated young men and women who wish to take part in its program. These centers will specialize in the education of nurses and doctors from among the native population. The students will be trained according to the highest standards possible in the locality, to meet the particular needs of the native populations.

Being acclimated, speaking the language, and being accustomed to native food and familiar with native customs, these young people, carefully trained, will be sent out not as individuals, but in organized groups under a head doctor or head nurse, to work from a common residence into the outlying districts to help the sick poor, with no distinction of race, creed, or color.

This community is now five years old, and already a notable group of young men have come to dedicate themselves to this work—among them doctors, nurses, and technicians. It is planned to establish the first center in a few years, and surveys are being made to determine the best place for a beginning.

Young men who experience a call to this work and are interested in medicine or nursing, or associated professions, are invited to write to me and secure further information. We are receiving frequent inquiries about the work, but we wish all the readers of THE JOURNAL to be informed as to this new and unique opportunity, and to receive this invitation to write for further details.

Rev. EDWARD F. GARESCHÉ, S.J.
Superior General
Sons of Mary, Health of the Sick
Sylva Maria, Salem End Road
Framingham, Mass.

USE OF ARTIFICIAL KIDNEY AFTER POISONING

To the Editor:—The April 13 issue of THE JOURNAL had a number of good articles on the problem of accidental poisoning. Although this may not strictly pertain to the first-aid management of poisoning, it should be realized that in very serious cases the use of the artificial kidney is definitely lifesaving. Berman and others (*J. A. M. A.* **161**:820-822 [June 30] 1956) have clearly documented its effectiveness. Their most dramatic case was that of a 28-year-old woman who took 25 mg. of phenobarbital. Dialysis was begun 49 hours after ingestion of the drug and repeated twice. Her life was saved.

Hemodialysis with the artificial kidney can clear the blood of intoxicants 5 to 20 times faster than fully functioning kidneys. (Schreiner and others: *New England J. Med.* **253**:213-217 [Aug. 11] 1955). When used by trained teams, the artificial kidney is a safe apparatus, as established by its use in over 1,000 cases. Compared to intestinal and peritoneal dialysis, it is much more efficient, according to Elkinton and Danowski in "The Body Fluids" (Balimore, Williams & Wilkins Company, 1955, p. 551). The use of this apparatus is

indicated in any serious poisoning from barbiturates, salicylates, thiocyanates, paraldehyde, methanol, bromide, and Doriden—as proved by actual experience.

Trained teams are available at Georgetown in Washington, under Schreiner; at Peter Bent Brigham in Boston, under Merrel and Guild; at the Cleveland Clinic, under Kolff; and at Bellevue in New York, under Morales. There are others, and a list is being compiled. The procedure would be to contact those in charge of the team, in order to determine if the dialysis is appropriate. Transportation should offer no serious problem. Even if artificial respiration has to be maintained during transportation, suitable apparatus is available (e. g., Jefferson ventilator by Air Shields, Hartboro, Pa.). When one considers that there are very few specific antidotes for most poisons, one can appreciate the value of the artificial kidney, which is capable of dialyzing a poison out of the body in as little as eight hours.

Jacob Greenblatt, M.D.
1675 Bedford St.
Stamford, Conn.

FLIGHT FOR FREEDOM

To the Editor:—I take this means of informing the members of the A. M. A., the New York Medical Society, the International College of Surgeons, and the hundreds of American doctors who had sent contributions to the American Medical Society in Vienna, to thank you all for the help which you have directly accorded me and my Hungarian colleagues.

I fled Hungary because the safety of myself and my family was in dire danger and because I knew the AVO would interrogate me and perhaps deport me, as they did so many others of our colleagues, to Rumania or Russia.

After having fled from Hungary we were accorded a heart-warming reception by the American Medical Society in Vienna, where each and every one of us received actual cash to restore our morale and help us over the immediate period of shock after having fled from our beloved country and our near and dear ones.

I do hope that you can find space to publish this letter to thank all of our American colleagues for their wonderful help and also to thank the American Medical Society of Vienna, particularly Mrs. Engel, for the encouragement, kind words, and practical aid which she and the society accorded us.

Dr. Judith Lehoczky
Hotel St. George, Room 707
Clark Street at Henry
Brooklyn 1, N. Y.

PREGNANCY AND THE MENSTRUAL CYCLE

To the Editor:—In Foreign Letters, The Journal, March 30, page 1174, there is a report on an article by Gold of Montreal. His original article, "The Relationship Between Length of Menstrual Cycle and Date of Delivery was published in the *Canadian Medical Association Journal* of Jan. 1, 1957, page 29.

In The Journal report it says: "His statistical analysis showed a consistent trend in the relationship between the length of the menstrual cycle and the duration of gestation." Nowhere in his discussion and summary does he mention "duration of gestation." He only discusses "length of menstrual cycle and the time of delivery."

Using his data, I confirm my own conclusions based upon my own data: the duration of pregnancy varies inversely with the length of the menstrual cycle. His data and mine, with ovulation dates from the graph by Riley, Dontas, and Gill in *Fertility and Sterility* of March-April, 1955, page 86, boil down to this: Three women, each with a last menstrual period beginning on Jan. 1, are due Oct. 8—Mrs. A, with a 35-day interval, ovulates Jan. 19½ and delivers Oct. 10; Mrs. B, with a 28-day interval, ovulates Jan. 14 and delivers Oct. 8; Mrs. C, with a 21-day interval, ovulates Jan. 8½ and delivers Oct. 6.

Women with longer menstrual intervals will carry past their due date (which is what Gold of Montreal concludes) but they will have had a shorter duration of pregnancy (as published by me in *Rocky Mountain Medical Journal* of June, 1956, page 541).

Lawrence T. Brown, M.D.
1134 Republic Bldg.
Denver 2.

TEACHING OF OCCUPATIONAL MEDICINE

To the Editor:—In the March 30, 1957, issue of The Journal, page 1139, the article "Is There a Doctor in the Plant?" reviewed some of the current activities of physicians devoting their efforts to occupational medicine.

The article stated that among recent developments there was this: "In California, medical school seniors are being oriented in industrial health problems, and a postgraduate course in occupational medicine is being discussed." I would like to point out that, in 1954, the committee on education and training of the Industrial Medicine Association conducted a survey of the medical schools of this country to determine if instruction in industrial medicine was included in the undergraduate curriculum. Of 63 schools which were queried, 48 replied, and, of this number, 39, or 81%, include material relating to occupational health in their curriculum. The emphasis is on the fact that a great number of schools are teaching this subject, and we wanted to correct the impression that one school only, and that being in California, has added this to the undergraduate program.

Several of the medical schools devote many hours in two or three of the undergraduate years, and this takes the form of didactic lectures, teaching seminars, field trips, creative experiences in patient examination, and exercises in job placement. The report of this committee appeared in *Industrial Medicine and Surgery*, August, 1954, page 360.

J. S. Felton, M.D.
Professor of Preventive Medicine
(Occupational Medicine)
The University of Oklahoma Medical Center
Oklahoma City 4.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Chiropractors: Injunction to Prevent Unlicensed Practice.—This was an action to enjoin the defendants from practicing chiropractic without a license. The defendants' motion to dismiss the complaint for want of equity was granted by the trial court and affirmed by the appellate court. The plaintiffs, therefore, appealed to the Supreme Court of Illinois.

The plaintiffs were licensed under the Illinois Medical Practice Act to treat human ailments without drugs or operative surgery, but the defendants, who engage in the same sort of practice and in the same county, were not so licensed. The plaintiffs alleged, therefore, that as a direct result of the defendants' activities the practice of the plaintiffs was limited and their income reduced. They also alleged that they had attempted on many occasions to procure prosecution of the defendants as provided by law but that these efforts had been unsuccessful and, further, that their licenses were in the nature of franchises conferring valuable property rights, which a court of equity should protect. As grounds for dismissing the plaintiffs' complaint, the defendants alleged that the plaintiffs had an adequate remedy at law by way of criminal prosecution.

The Supreme Court first pointed out that it is a fundamental principle that courts of equity do not have jurisdiction to enjoin the commission of a crime. An exception has been made to this general rule in situations like the present one, however, under either of the following theories: (1) that the license is a franchise in the nature of a property right, which equity will protect; or (2) that the unlicensed practice of chiropractic constitutes a public nuisance, which equity will abate. In an early Illinois case, the Supreme Court refused to enjoin a group of unlicensed chiropractors from practicing in the state. Later cases in other states have allowed an injunction in such cases, however, and the Supreme Court said that there are sound, compelling reasons for abandoning its former position.

In the first place, one holding a limited or full license to practice medicine has a "property right" in the sense that laws affecting him in his practice must satisfy due process of law. The license confers a right in the nature of a franchise in that it grants the privilege of doing that which does not belong to the public generally by common right. In this regard, the license to practice medicine, which is conferred only for merit, differs from an ordinary, regulatory license, such as a tavern license, a revenue license, or an automobile license. To qualify for a license to practice the healing art, the licensee must meet high standards, established for the purpose of protecting the public health, morals, safety, and welfare. Whether the right to practice the profession be called a franchise, a license, or a privilege, it is, said the Supreme Court, a valuable right that should, in justice, be entitled to protection. Since the practice of chiropractic in the state by one who is not licensed constitutes an infringement of the rights of those who are properly licensed, the latter may secure relief against such unlawful practice in a court of equity.

In the second place, the court said that the prevention of unlicensed practice of chiropractic benefits the public as well as the plaintiffs, because it helps insure compliance with those laws that the court has sustained as a reasonable exercise of the legislature's police power in protecting the public health and welfare. Although the legislature could have provided for injunctive relief, its failure to do so does not preclude a court from acting. Accordingly, the judgment of the appellate court in favor of the unlicensed practitioners was reversed. *Burden v. Hoover, 137 N.E. (2d) 59 (Ill., 1956).*

Pharmacists: Liability for Filling Prescription from Improperly Marked Bottle. The defendant, a licensed pharmacist, was charged with manslaughter for allegedly deviating from the terms of a physician's prescription, resulting in the death of the physician's patient. From a judgment of conviction, the defendant appealed to the Supreme Court of California.

The defendant was employed as a pharmacist by the Ethical Drug Company of Los Angeles. On July 6, 1954, he filled a prescription written by a licensed physician and presented by a customer of the store. The prescription called for "Sodium phenobarbital, grains eight. Sodium citrate, drams three. Simple syrup, ounces two. Aqua peppermint, ounces one. Aqua distillate QS, ounces four." The defendant assembled all of the necessary ingredients and prepared the prescription, which was given to the customer. The customer put a teasponful of the prescription in his baby's milk and gave it to the baby. The child died a few hours later. A few months later another pharmacist in the store prepared an identical prescription, which was given to another child. That child became seriously ill but did not die. Both children were diagnosed as suffering from methemoglobinemia caused by the ingestion of nitrite, and it later developed that the bottle from which the sodium citrate was taken had apparently at one time contained sodium nitrite, because a chemical analysis of the prescription disclosed the presence of sodium nitrite and washings from the cap of the bottle did also. The evidence indicated that no one had put sodium nitrite in the bottle since the present store owner bought the store in 1950 and that the bottle was a part of the original inventory. Further, there was nothing in the record to indicate that the contents of the bottle labeled sodium citrate could have been identified as containing sodium nitrite. There was testimony that at first glance sodium citrate and sodium nitrite are identical in appearance, that in form either may consist of small colorless crystals or white crystalline powder, that the granulation of the crystals may vary with the manufacturer, and that there may be a slight difference in color between the two. A chemist further testified

that the mixture did not appear to be homogenous but that, from visual observation alone, he could not identify the crystals as one substance or the other.

The court first pointed out that there was no evidence whatever that would justify an inference that the defendant knew or should have known that the bottle labeled sodium citrate contained sodium nitrite. On the contrary, the undisputed evidence showed conclusively that the defendant was entirely morally innocent and that only because of a reasonable mistake or unavoidable accident was the prescription filled with a substance containing sodium nitrite.

The Supreme Court said that in order to be guilty of manslaughter a criminal intent must be shown. If, continued the court, the person who committed the act or made the omission charged was acting under an ignorance or mistake of fact, he has no criminal intent and is incapable of criminal negligence. This is also true of persons who commit an act through misfortune or by accident, when it appears that there was no evil design, intention, or culpable negligence. The California statute imposing strict liability upon those who prepare, compound, or sell adulterated or misbranded drugs does not apply to one licensed to dispense drugs who does so with due caution and circumspection. The defendant, said the court, was committing a lawful act in filling the prescription, and neither intentionally nor through negligence did he prepare compounds or sell adulterated or misbranded drugs. Furthermore the court said that, even though the defendant was ignorant of the true contents of the bottle marked sodium citrate, he did not act ignorantly in filling the prescription because he had the professional knowledge and skill necessary. The intention of the legislature was to force care and caution on the part of dealers in drugs, and the defendant exercised such care and caution because he had a right to rely upon the fact that the bottle marked sodium citrate did in fact contain sodium citrate and not something else. The judgment of conviction was accordingly reversed, the court holding that the defendant acted with due care and caution and not ignorantly. *People* v. *Stuart, 302 P. (2d) 5 (Calif., Oct., 1956.)*

Malpractice: Sufficiency of Evidence.—This was an action for damages alleged to have been caused by the negligence of the defendant surgeon during a mastoidectomy. From directed verdict for the defendant, the plaintiff appealed to the Court of Appeals in Maryland.

When the plaintiff was 7 years old (this suit was filed within three years after he became of age), he entered a hospital with a diagnosis of convalescent chickenpox and scarlet fever. He had a purulent discharge from his right ear, which did not respond to sulfanilamide, and on the 27th hospital day a mastoidectomy was performed. The hospital record contained a summary of history notes, which stated, among other things, "The mastoid was in such a necrotic state that considerable excavation was necessary. During the operation the facial nerve was found." The patient recovered from the operation fairly well, and no abnormalities were noted. On the following day, however, a fairly marked paralysis of the right side of the face was evident.

The defendant admitted that he had forgotten most of the details after the lapse of 18 years, but he stated positively that there was no nerve injury at the time of the operation. The record showed that the paralysis did not appear until about 18 hours later, and the defendant stated that, if the plaintiff's facial nerve had been injured or severed at the time of the operation, there would have been an immediate nerve paralysis. He admitted that a nerve may be compressed by too tight packing, which might result in a paralysis later, but he insisted that the plaintiff's wound was not packed too tightly. The medical expert called by the plaintiff also stated that, if damage is done to the facial nerve during an operation, the result would be "noticeable immediately," and he added that, if paralysis appeared 18 hours later, he would redress the wound as the defendant did. He also pointed out that a facial paralysis may result from a head cold, a severe infection, an allergic reaction, and other causes.

It is clear under the Maryland authorities, said the Court of Appeals, that in an action for malpractice the burden of proof is upon the plaintiff to show a want of proper knowledge and skill. The doctrine of *res ipsa loquitur* does not apply. Negligence cannot be inferred from the occurrence alone. We think, continued the court, that there was no testimony that the facial nerve was severed. The defendant explicitly denied it, and there was circumstantial evidence strongly supporting the conclusion that had the nerve been severed the paralysis would have been observed at the time of, or at least shortly after, the operation. Furthermore, the statement in the hospital record that the nerve was found or exposed is far short of saying that it was severed. The Court of Appeals, therefore, found no error in the action of the trial court in directing a verdict for the defendant, and the judgment for the defendant surgeon was affirmed. *Bettigole* v. *Diener, 124 A. (2d) 265 (Md., 1956).*

Court's Right to Require Plaintiff to Submit to a Physical Examination.—This was a petition for a writ of mandamus to compel the respondent judge to expunge an order he had made requiring the petitioner to submit to a physical examination. It was an original action heard by the Supreme Court of Illinois.

The petitioner was the plaintiff in a personal injury action. Defendant in that action filed a verified petition in which he alleged that he needed information as to the nature and extent of the plaintiff's injuries in order to prepare for trial and that he had no means of getting that information without an independent physical examination of the plaintiff. His request for an order requiring the plaintiff to submit to a physical examination by a physician chosen by him, with all incidental expenses to be borne by him, was granted by the respondent, the judge hearing the motion.

The petitioner contended that the court did not have the power to direct him to submit to a physical examination. There have been a number of cases in Illinois in which it was said that courts lack the

power to require a plaintiff in a personal injury action to submit to a physical examination. In none of these cases, said the Supreme Court, is any reason for asserted lack of the power stated, and the problem has never been analyzed. Many of the decisions that held that a court lacked the power to require a physical examination also pointed to circumstances that would have made the exercise of the power inappropriate if it existed. The common law, from earliest times, permitted and required physical examinations when they were necessary. Courts of other states have recognized an inherent power to require examinations when required by the ends of justice.

It is possible, said the court, that strong feelings as to the "inviolability of the person" may have been tacitly responsible for the previous handling of the problem. The court said, however, that one who seeks to recover damages for physical injuries puts his physical condition in issue and it is as much a fact to be proved as the conduct that caused the injuries. The basic principle of the law of evidence is that what is relevant is admissible, and any exception to this principle must justify itself. If there is to be an exception here, it must be because a privilege exists. A privilege in the law of evidence, to be soundly based, must rest on considerations that make it more desirable to risk concealment of the truth than to disrupt the values that the privilege supports. No such considerations are involved in the ordinary physical examination in a personal injury case.

It is also possible, the court continued, that the doctrine of "lack of power" may have been a shorthand way of saying that the court felt that it was appropriate for the legislature, and not the courts, to determine that such examinations should be permitted. This view, said the court, ignores the common law precedents that permitted physical examination where necessary and overlooks the power of courts to regulate judicial procedure. It also involves the dubious assumption that the legislature today could cut off constitutionally a reasonable and appropriate method of getting at the truth in a judicial proceeding. Formerly, the adversary aspects of a trial were emphasized, but now the emphasis is on the role of a trial as a search for truth. Limited discovery, available only in equity, has been replaced by comprehensive discovery available in all actions; in view of this, it would be difficult to justify an exception that would single out for disparate treatment a plaintiff seeking damages because of his physical condition. Physical examination is almost everywhere permitted in appropriate cases. The court said that the time had come for it to recognize the propriety of requiring plaintiffs to submit to physical examinations in appropriate cases. It was appropriate to order a physical examination in this case. The defendant needed information therefrom to prepare for trial, the physical examination would not involve any unusual physical hazard, the examining physician was competent, the time and place of the examination were reasonable, and the defendant was to bear all expenses. Accordingly, the prior decisions holding that courts lacked the power to require such examinations were overruled, and the petition for a writ of mandamus was denied. *People ex rel. Noren v. Dempsey, 139 N. E. (2d) 780 (Ill., 1957).*

Chemical Tests for Intoxication: Proper Qualification of Expert Witness.—The defendant was charged with the offense of driving a motor vehicle on a public highway while under the influence of intoxicating liquor. From a judgment of conviction, the defendant appealed to the criminal court of appeals of Oklahoma.

At the trial, a state highway patrolman testified that the defendant was taken to the sheriff's office after the accident and there was given an Intoximeter test. One H. L. Spencer then testified that he had been employed as a chemist and biologist at the Medical Arts Laboratory, Tulsa, Okla., for 10 years, that he had a master's degree from the University of Kansas and that he was familiar with the Intoximeter test and had been analyzing the particular kind of kit used in the test for about five years. In fact, he said he prepared a certain number of the kits for the highway patrol. He described in detail the preparation of the kits and the final test when the kit is returned from the highway patrol. He analyzed the defendant's breath sample and found that it tested 0.1636. Another witness, Dr. William Van Pelt, testified that he had spent four years at the University of Arkansas School of Medicine and was a graduate, that he was familiar with studies in connection with the effect of alcohol in the human system, and that he was the city police physician, had been called on to study and to testify in cases in which the intoximeter was used, and was familiar with the standards set up by the American Medical Association on the effect of alcohol. In his opinion the percentage of alcohol necessary to be found in a person's blood before it can definitely be said that such person is intoxicated is 0.15.

The defendant contended that the qualifications of Mr. Spencer to testify as an expert were not established. His counsel argued that the witness was not competent to testify as to the amount of alcohol contained in the blood of the defendant on the basis of having examined a breath sample. It is improper, he said, for a chemist to use an "empirical formula" prepared by others—it is likewise hearsay. On cross-examination the witness had admitted that, in translating the results of the breath test into amount of alcohol in the defendant's blood, he had used a formula that was furnished with the Intoximeter. "That is just a formula that has been taken; that is not my own determination, as such, insofar as I have checked on the same individual, blood alcohol and one of these tests; at the same time, I have confirmed in my own mind that the thing works."

The court said that since the chemist had confirmed the formula in his own mind, the trial court properly ruled that he was an expert witness and that his testimony was admissible in evidence. Other contentions of the defendant were also overruled, and the judgment of conviction was affirmed. *Bryant v. State, 302 P. (2d) 787 (Okla., 1956).*

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Thrombocythemias. J. Bousser, J.-J. Benhamou, D. Christol and M. Mas. Presse méd. **65**:347-351 (Feb. 23) 1957 (In French) [Paris].

Thrombocythemia is a condition characterized by a permanent increase in the number of platelets, accompanied by significant hyperplasia of the megacaryocytes of the marrow. Thrombocytosis, on the other hand, is characterized by a temporary increase in platelets. Thrombocythemia may be primary or secondary. The term "essential thrombocythemia" should be restricted to primary thrombocythemia for which no definite cause can be found. The other primary forms of the condition are those found in association with myeloid leukosis and, especially, with polyglobulism. The principal causes of secondary thrombocythemia are splenectomy and osseous metastases.

Essential thrombocythemia is rare. A search of the literature revealed reports of 31 cases, published under several different designations, to which the authors add one of their own. The patient, a 53-year-old woman, sought advice for osseous pains of about 1 year's duration, which had begun in the arms and had subsequently spread over the whole skeleton. Questioning brought out the fact that a significant hemorrhagic syndrome, with epistaxis, bleeding of the gums, and ecchymoses, had also begun about a year before. Clinical examination showed enlargement of the spleen, a normal liver, and no involvement of the lymph nodes. The blood cell counts showed 6,120,000 red blood cells, 17,000 white blood cells, and 2,600,000 platelets per cubic millimeter. Capillary fragility, a prolonged bleeding time, and hypoprothrombinemia were revealed by the laboratory tests. Thromboplastin formation, however, was not above normal in spite of the thrombocytosis. Administration of 6 mc. of phosphorus-32 (P^{32}) produced a striking improvement in the patient's condition. The bone pains disappeared within a fortnight, and by the end of 3 months the spleen was no longer palpable. Hematological studies showed that the leukocytosis and thrombocytosis were no longer present. Seven months later, the red blood cell and platelet levels began to increase again but were brought back to normal by the administration of an additional 4 mc. of P^{32}. Follow-up of the patient 2½ years after her first examination showed that the blood findings had remained normal.

P^{32} is the therapeutic agent of choice for essential thrombocythemia. Its administration results in a rapid return of the platelets to normal levels and leads to the disappearance of all the other disturbances, especially the hemorrhagic syndrome. Recurrences sometimes make it necessary to administer a 2nd dose. The prognosis is generally favorable, and survivals of 5, 10, or more years are frequent. Thrombocythemia is often associated with polyglobulism, and the many intermediate forms found between essential thrombocythemia and essential polyglobulism suggest that essential thrombocythemia is only 1 form of a type of myeloproliferation that usually results in polyglobulism.

Aetiology and Localisation of Lung Abscess: An Analysis of Forty Cases. L. M. Sanghvi. J. Indian M. A. **28**:187-190 (Feb. 16) 1957 (In English) [Calcutta].

Of 40 patients between the ages of 11 and 60 years with abscess of the lung, 39 were male and 1 was female. Thirty-three belonged to the lowest income class. Pneumonia and infection of the upper part of the respiratory tract were the commonest causes. Dental infections played little part in the causation of the disease. Localization of the abscess was determined by posterioanterior and lateral roentgenograms. The upper lobe and the apical segment of the lower lobe of the right lung were the sites most frequently involved. The anterior segment of the upper lobe and the middle lobe of the right lung were more frequently involved in this series than in those reported by other workers. A possible explanation for this was suggested, when, in an investigation of the posture during sleep of 500 hospitalized patients, 30% of them were seen to be asleep in a posture markedly rotated towards the prone position.

Hæmophilia B and Its Treatment. F. Heni and I. Krauss. German M. Month. **2**:55-57 (Feb.) 1957 (In English) [Stuttgart, Germany].

Of 14 patients with hemophilia who were members of different families and who were studied in the course of the last few years, 3 had hemophilia B (Christmas disease, deuterohemophilia). Of the 3 patients, 2 were men aged 41 and 30 years respectively, and 1 was a 12-month-old baby boy. Biggs' thromboplastin generation test revealed absence of the plasma thromboplastin component (Christmas factor). The treatment of severe hemorrhage in patients with hemophilia B consists of blood transfusion, since the missing factor itself has not yet been isolated in pure form. Experience has shown that serum contains the plasma thromboplastin component in a more

The place of publication of the periodicals appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individuals in continental United States or Canada who subscribe to its scientific periodicals. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover 1948 to date only, and no photoduplication services are available. No charge is made to members, but the fee for others is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

active form than does whole blood. The intravenous infusion of serum is, therefore, more effective in arresting hemorrhage than is transfusion of either fresh or stored whole blood. The 1st of the 3 patients urgently required extraction of 4 teeth because of recurrent, severe, and painful alveolar abscesses. After intravenous infusion of 200 cc. of serum, the clotting time remained normal for about 36 hours, but after 48 hours it was again prolonged by 20 minutes. The prothrombin consumption time returned to normal when at least 200 cc. of serum had been given, and it was only moderately improved by smaller amounts of serum, although the clotting time of whole blood was normal. It was possible to extract the 4 teeth with the aid of the serum transfusions, but, after serum had been given for the 9th time, the clotting time could not be reduced to less than 18 minutes and the prothrombin consumption time remained slightly abnormal. This indicates that in hemophilia B, as in hemophilia A, antibodies against plasma thromboplasmin may develop.

Treatment of Polyarteritis Nodosa with Cortisone: Results After One Year. Report to the Medical Research Council by the Collagen Diseases and Hypersensitivity Panel. G. W. Pickering, E. G. L. Bywaters, J. F. Danielli and others. Brit. M. J. 1:608-610 (March 16) 1957 [London].

A series of 17 patients with periarteritis nodosa proved by biopsy and a retrospective control series of 19 patients with the same disease are reported on. The diagnostic indexes of all patients with periarteritis nodosa proved by biopsy admitted to the hospitals from 1946 until the introduction of cortisone therapy in 1950, which group contained most of the treated patients, had been collected to obtain a retrospective control. The assessment of therapeutic activity by the use of retrospective controls may be fallacious and is not a valid substitute for the strictly controlled clinical trial. The severity of the constitutional illness appeared to be similar in the 2 groups. The chief difference was in the incidence of hypertension. Eight of the untreated patients but only 1 of the treated group had hypertension at the time of biopsy. Periarteritis started in the treated patients in 1950 and in the untreated patients between 1941 and early 1950. The initial effects of cortisone therapy were dramatic, but a complete suppression of the outward manifestations could be maintained only in 3 of the 15 survivors 6 months after treatment with cortisone was started. This suppression required large doses of the drug, which provoked troublesome and occasionally dangerous side-effects. One year after biopsy, 7 of the 19 untreated patients were still alive, as compared with 14 of the 17 treated patients. Active periarteritis nodosa had ceased in 2 untreated and in 4 treated survivors. One of the treated patients was still receiving small doses of cortisone, but there was no recurrence of activity, when treatment was discontinued 3 months later. The interval from biopsy to death ranged from 1 week to 7 months in the untreated patients and from 1 to 11 months in the treated patients.

No unequivocal evidence is presented to show whether treatment with cortisone is better or worse than the disease itself. Final conclusions about the effect of cortisone on life expectancy in patients with periarteritis nodosa cannot yet be made, although, according to the results, treatment with cortisone may prolong life.

A Study Comparing the Effects of Bed Rest and Physical Activity on Recovery from Pulmonary Tuberculosis. J. G. Hirsch, R. W. Schaedler, C. H. Pierce and I. M. Smith. Am. Rev. Tuberc. **75**:359-409 (March) 1957 [New York].

The beneficial effect of bed rest on recovery from tuberculosis was widely accepted prior to the introduction of effective chemotherapy, but how much bed rest is necessary now with chemotherapy? The answer to this question is important not only to the patient and his physician but also to those responsible for planning facilities and procedures for the care of patients with tuberculosis. During the past 2 years the authors attempted to assess the role of bed rest in treating a small number of tuberculous women. Instead of treating alternate patients in different fashion, each patient was alternated through periods of bed rest and of physical activity, and detailed clinical and laboratory observations were made to determine whether or not physical activity would be reflected in clinical worsening or at least in slowing the rate of recovery. Thus, each patient served as her own control. The patients had moderately far-advanced or far-advanced pulmonary tuberculosis thought to be of recent origin. None gave a history of earlier treatment for tuberculosis. They were consecutive admissions, except for 2 patients who were eliminated from the study because pretreatment cultures revealed tubercle bacilli highly resistant to streptomycin, isoniazid, and aminosalicylic acid.

The antimicrobial regimen used consisted of 1 Gm. of streptomycin sulfate given intramuscularly 3 times a week and 5 mg. of isoniazid per kilogram of body weight given daily. In some patients in whom drug resistance was encountered, aminosalicylic acid was substituted or added. During the bed-rest phase, patients were confined to their beds except for a maximum of 4 brief visits daily to the lavatory. At mealtime the Gatch bed was elevated. At all other times the patients were required to lie flat in bed. The only activities permitted were reading and listening to the radio. The active phase was also rigidly supervised. During this phase the patients cared for personal toilet and took tub baths. They had breakfast at a table, after which they helped to clean the table and dishes. After breakfast they were required to "house-clean" their individual bedside units and make their beds. A half-hour of calisthenics included arm movements, trunk flexing, and deep knee bends, and this exercise was followed by 2 hours of occupational therapy. Lunch was followed by cleaning-up of dishes and tables and then by rest in bed for 1 hour. Then, another hour of occupational therapy followed. During the following 2 hours (visiting period) they had a choice of playing cards, dancing, watching television,

or playing volley ball. Supper and cleaning up of dishes and table was followed 1st by one-half-hour of group exercise and then by bed rest for 1 hour. After that there was free choice of activity, including occupational therapy. Patients retired at 10 p. m. and slept till 7 a. m. Detailed clinical and laboratory observations revealed no detectable deleterious effect of physical activity on the course of recovery.

Sodium and Potassium Content of the Serum During Addisonian Crisis in Patients with Adrenal Cortical Hypofunction. F. Schwarz. Nederl. tijdschr. geneesk. 101:442-445 (March 9) 1957 (In Dutch) [Haarlem, Netherlands].

Patients with adrenal cortical hypofunction who go into crisis usually show, in addition to the well-known clinical symptoms, such as low blood pressure level, muscular weakness, gastrointestinal disturbances, and psychological changes, biochemical changes, such as reduction in the sodium and increase in the potassium content of the serum. This, however, is not always the case, for the author observed 3 patients with typical clinical signs of addisonian crisis in whom there were no decided deviations in the serum electrolyte levels. Two of these patients had adrenal cortical hypofunction, and the 3rd had undergone bilateral adrenalectomy for the treatment of carcinoma of the breast. Studies of these 3 patients revealed that the sodium and potassium concentrations in the serum were only slightly disturbed. The author shows that this is in agreement with experimental studies carried out by others and that it indicates that disturbances in the water and electrolyte metabolism are not of dominant influence in the pathogenesis of addisonian crisis.

The diagnosis of crisis should not therefore be made on the basis of the sodium and potassium contents of the serum of patients with adrenal cortical insufficiency. Furthermore, it is necessary to reexamine the advisability of giving large amounts of water and desoxycorticosterone acetate in patients such as those reported here. These should receive intravenous infusions of an alcoholic suspension of hydrocortisone in 0.9% solution of sodium chloride (100 mg. in 1 liter). An intramuscular injection of 50 mg. of cortisone acetate should be given at the same time. With this form of treatment the author was able to obtain favorable results.

Infectious Mononucleosis and Antibiotic Therapy. J. S. Lumio. Acta oto-laryng. 47:251-257 (March) 1957 (In English) [Stockholm].

Of 395 patients, 173 female and 222 male, between the ages of 8 months and 40 years with infectious mononucleosis, 292 received antibiotic therapy and 103 were treated without antibiotics. In agreement with earlier investigations, 203 (51.4%) of the 395 patients were between the ages of 16 and 25 years. Only 4 patients were afebrile throughout the course of the disease. Acute pharyngitis was observed in 381 patients (96.5%), and 347 (87.9%) had pseudomembranes. Of 12 patients whose tonsils had been removed, 6 had marked pseudo-membranes covering the posterior wall of the pharynx, 4 showed marked inflammation of the pharynx without pseudo-membranes, and 2 had a normal appearing pharynx. Of 350 patients on whom the Paul-Bunnel heterophile agglutination test was performed, 127 had a negative reaction, and 223 (63.7%) had a positive reaction in dilutions of 1:64 or over. Of the 292 patients treated with antibiotics, 256 received penicillin alone in doses of 450,000 or 600,000 units a day for from 5 to 7 days, 26 were given penicillin combined with chlortetracycline, chloramphenicol, or oxytetracycline and 10 were given chlortetracycline, chloramphenicol, or oxytetracycline without penicillin.

The febrile phase in those treated with antibiotics lasted an average of 11 days, and these patients were hospitalized for 7 days. The corresponding figures for patients who did not receive antibiotics were 10 and 7 days. Consequently no significant difference was observed between these 2 groups. Three (1%) of the 292 patients treated with antibiotics had a bacterial infection. Similarly, bacterial complications occurred in 3 (3%) of the 103 patients treated without antibiotics. These data suggest that, although antibiotics do not exert an effect on the infectious mononucleosis, their administration is to be recommended for the prevention, at least to some extent, of complications, especially when the patients are exposed to secondary infections during therapy.

Weight Reduction in Obese Young Men: Metabolic Studies. C. M. Young, E. L. Empey, V. U. Serraon and Z. H. Pierce. J. Nutrition 61:437-456 (March) 1957 [Philadelphia].

Nitrogen, calcium, and phosphorus metabolism on a constant intake of the three nutrients was studied in 8 obese young men by means of 7-day balance studies during a prereduction period of weight maintenance, at the 4th and 8th weeks of weight reduction, and at the 4th week of postreduction weight maintenance. Weight losses in the 8-week reducing period ranged from 13.4 to 27.5 lb. with a mean of 22.6 and a median of 23.6 lb. Weight losses appeared to be related to initial body weights. Four of the 8 subjects went from nitrogen and phosphorus retention or equilibrium in the prereducing period to nitrogen and phosphorus loss during the period of caloric restriction. Within the limits of the experiment, the losses did not appear to increase with prolongation of the reducing period. Relief of caloric restriction was accompanied by return to equilibrium or retention with respect to these nutrients, but at a lower level. In contrast to women subjects studied previously, only 3 of the 8 men went into calcium deficit and the deficit occurred early in the weight reduction period with subsequent return to calcium equilibrium in the later stages of reducing. No satisfactory explanation is given for the changes in calcium retentions. In 7 of the 8 subjects, 24-hour basal caloric requirements decreased during weight reduction; the mean decrease was 150 calories or 8.4%.

On Outbreak of Trichinosis in Ireland in 1956. J. Nash, J. G. Kidney, M. J. G. Furnell and P. B. O'Meara. J. Irish M. A. **40**:74-76 (March) 1957 [Dublin].

An outbreak of trichinosis in Tipperary North Riding and the symptoms of 7 patients (1 of whom died) are recorded. Three of the patients admitted to either eating or nibbling at raw sausage. All patients were women ranging in age from 17 to 50 years, and all had contact with pork products either as cooks or as handlers of pig meat. The factory from which the sausages in 3 cases were derived had an excellent record. Diligent enquiries, investigation of rat infestation, and examination of meat prepared for sausages were all negative. One of the patients died of a pulmonary embolus, and it had to be determined whether the death was simply due to bed rest in an obese woman with pyrexia or whether the death could be directly attributed to trichinosis. The patient had initially complained of pain and soreness in the legs. In a Liverpool epidemic a patient died of a pulmonary embolus in the 3rd week of the illness. Another patient died apparently of inflammation and necrosis of the myocardium. Three other patients had sudden attacks of dyspnea in the 3rd week of the illness, and 1 of them had edema of the legs. Activity that might put undue strain on the myocardium should be avoided, but patients should not be confined to bed, particularly during the 3rd week of the disease. Severely ill patients with obesity or varicose veins and those liable to venous thrombosis might be treated with anticoagulants.

No specific treatment was given to any of the patients, but symptoms were relieved by analgesics and sedatives. Most patients complain of swelling of the eyes or face, muscular pains, headache, and photophobia and have an initial high temperature. The combination of the above symptoms and eosinophilia strongly suggest trichinosis. Muscle biopsy is the most reliable confirmatory test. In man, the concentration of the Trichinella larvae is highest, in descending order, in the tongue, diaphragm, forearm, calf, and thigh muscles. In practice, specimens should be taken from the outer aspect of the thigh.

A Statistical Study on 631 Subjects with Tetanus. F. Recchia. Aggiorn. mal. infez. **2**:359-372 (Nov.-Dec.) 1956 (In Italian) [Rome].

In a series of 631 patients, mostly males, with tetanus, 424 were 13 years of age or older and 201 were under 13, and in 6 the age was unknown. Seven newborn babies died of tetanus, probably as the result of umbilical cord infection. Peasants constituted 26.8% of the patients. Eighty-five of the 201 children lived in rural areas, 36 in small towns, and 80 in large cities. Of the 195 patients who contracted tetanus in the summer, 86 died; of the 177 who were infected in autumn, 72 died; of the 147 who were infected in the spring, 47 died; and, of the 112 who were infected in the winter, 44 died. No observable lesion was present in 368 patients. Generalized tetanus occurred in 550 patients, splanchnic in 8, monoplegic in 3, paraplegic in 2, and cephalic in 68.

SURGERY

Hexachlorophene in the Surgical Scrub. I. Havens, R. R. Benham and D. E. Clark. Am. J. Med. Technol. **23**:76-86 (March-April) 1957 [Houston, Texas].

An attempt was made to define both the concentration of hexachlorophene and the pattern of usage that would give the best results in surgical scrubbing with commercially available cleansing agents containing this agent. No inhibitory effect of hexachlorophene was evident after a single scrubbing. The continued use of this agent in a sufficient concentration resulted in a marked decrease in the number of viable bacteria that could be removed from the hands. A preparation containing in the dilution used 0.7 to 0.9% of hexachlorophene and 8 to 10% of soap solids appeared to be optimal for use in surgical scrubbing. A reduction in the bacterial count of over 90% for a 4-minute scrub was obtained, compared to a reduction of 82% for the standard 10-minute scrub with a benzalkonium chloride soak. Consideration of such other factors, as alkalinity, tactility, odor, and color will be important in compounding a product satisfactory to all users.

Tracheotomy—Then What? R. L. Rapport, J. P. Rahm and G. Curry. Am. J. Surg. **93**:550-557 (April) 1957 [New York].

Of 159 tracheotomies performed between 1946 and 1955, 59 were indicated for nontraumatic conditions. Twenty-eight tracheotomies were performed on patients with poliomyelitis. Of 112 tracheotomies performed between 1953 and 1955, 90 were performed in seriously injured persons. Fifty-two tracheotomies (33%) were performed on admission, 100 (64%), including the 52, were performed within the first 12 hours after admission, 26 (15%) between 12 and 48 hours, and 33 (21%) after 48 hours. Tracheotomy should be performed when it is first considered. Delay of even a few hours may endanger the patient's life. Delays of 6 days or more were due to late development of complications, such as pneumonitis, atelectasis, mediastinitis, and tetanus.

In recent years the indications for tracheotomy have been extended so that this is now a commonly performed procedure. Difficulties arise not so much from the time and method of performing a tracheotomy as from inadequate care once the operation has been performed. Detailed explanation should be given the conscious patient concerning why tracheotomy is to be performed and the necessity for aspiration in order to prevent serious mental trauma. It is essential that personnel be thoroughly trained in the technique of aspiration. The catheter coudé should be used for aspiration because its curved tip facilitates catheterization of the left main bronchus. The catheter, when not in use, should remain in a solution of aqueous benzalkonium chloride, and the catheter should always be moistened before use to avoid undue trauma. A Y-tube should be introduced into the aspirating system so that the vacuum can be released immediately by fingertip control. The inner cannula should always be inserted after introduction of the tracheotomy tube. It should be removed and cleansed

as necessary in order to prevent encrustations and plugs. After establishment of a tract at the end of 3 days, the entire tube should be removed and replaced daily. When the time for extubation approaches, replacement of the tracheotomy tube with progressively smaller ones is to be preferred to trial occlusion. The smallest tube may then be corked before final removal. A special ward should be established for the care of tracheotomized patients. It is essential that the teaching program be directed toward student and graduate nurses, interns, residents, and attending staff. For supplementation of the training program and for assurance of more adequate tracheotomy care, instructions are placed at the bedside of each patient. By these methods, errors commonly made will be avoided and the management of patients with tracheotomies will be improved.

Missiles Lodged in the Heart. E. Hasche. Thoraxchirurgie 4:432-442 (Feb.) 1957 (In German) [Stuttgart, Germany].

Of 100 patients with missiles lodged in thoracic organs, in 65 missiles were in the lung and in 15 in the heart. Of the latter only those that had been lodged for some time were considered. Ten of the 15 patients complained of piercing pains in chest or precordium, 8 of intermittent dyspnea, 6 of a sensation of pressure or of oppressive anxiety, and 2 of angina pectoris. Objective signs were: tachycardia in 2, arrhythmia in 2, pathological changes in the electrocardiogram in 7, and physical changes in 3. Roentgenologic studies permitted localization of the missiles: in the wall of the right auricle in 1 patient, in the wall of the right ventricle in 2 patients, in the wall of the left ventricle in 3 patients, and in the pericardium or the pericardial space in 9 patients. There were no characteristic electrocardiographic changes, but occasionally there were signs of functional impairment of parts of the myocardium.

Although formerly some surgeons believed that all missiles lodged in the heart should be removed, this view is no longer accepted, but sequels necessitating removal may arise years later. Flare-up of an infection in the surroundings of a shell splinter, the threat of an embolism when a missile located in a ventricle is carried into the circulation, the development of an aneurysm in the wall of the heart, and the development of pleuropericardial or pericardial adhesions may require the removal of the missile. In 5 of the 15 patients reviewed here, operation was deemed necessary. A missile was removed in 1 from the wall of the right ventricle, in 2 from the wall of the left ventricle, and in 2 from the pericardium. One patient from whom a shell splinter was removed from the wall of the left ventricle died as the result of postoperative pericardial tamponade. The other 4 patients recovered. Complications that may result after the removal of a missile lodged in the heart are: postoperative hemorrhage from the bed of the missile or from the suture, flare-up of an infection, the formation of an aneurysm in the suture, or the development of adhesive pericarditis.

Treatment and Its Results in 1,130 Fresh Closed Fractures of the Shafts of the Leg Bones. J. Ender, H. Krotscheck and H. Jahna. Monatsschr. Unfallh. (Supplement 54) pp. 14-92, 1957 (In German) [Berlin].

This is one of a series of reports on 3,308 leg fractures. The 1,130 new, closed fractures of the leg reviewed in this paper were in 1,123 patients. There were 311 isolated fractures of the shaft of the tibia and 819 fractures of both bones of the leg. Classification of fractures revealed connections between fracture healing and such factors as age of the patient, form of fracture, and extent of displacement of the fracture ends. The majority (970 patients) received conservative therapy, being treated either with a plaster cast or with extension and subsequently with a walking cast. Transfixation was used in 65 patients, medullary nailing in 65, and osteosynthesis in 17 patients. Detailed analysis revealed the superiority of conservative over the operative treatment.

Fifteen deaths occurred during the period of hospitalization in the 1,123 patients, but only 3 of the deaths resulted (indirectly) from the fracture, 2 being caused by pulmonary embolism and 1 by encephalitis. Two amputations were necessary, 1 because of infection after medullary nailing and the other because of gangrene of the foot in a patient who was hospitalized on the 6th day after fracture, when gangrene had already begun. Pseudarthrosis developed in 2 patients. In 40 patients fracture healing was retarded in that more than 140 days (average, 201) was required for healing. A total of 477 patients or 45% were reexamined from 2 to 25 years after the fracture was sustained. Hard labor was being performed by 170 or 30% of the reexamined patients. Only 10 patients had found it necessary to change their occupation, and the average age of these was over 50 years. The gait was normal in 400 of the 477. The 63 who complained that their walking capacity was impaired had an average age of 59 years. Fifty-five of the 554 patients who sustained their fractures in their occupations received a permanent disability pension, and 34 of these were over 50 years of age.

Treatment and Results in 461 Fresh Open (Compound) Fractures of the Shafts of the Leg Bones. G. Zrubecky. Monatsschr. Unfallh. (Supplement 54) pp. 93-180, 1957 (In German) [Berlin].

This report is concerned with 461 fresh, open fractures of the shafts of the leg bones in 456 patients, 5 having open fractures of both legs. Of the 24 deaths in this group, 4 were due (indirectly) to the fractures (2 from pulmonary embolism and 2 from sepsis), and the other 20 were due to other injuries sustained simultaneously with the open fracture of the leg. Primary amputation was necessary in 31, and secondary amputation in 12 patients. Wound infection developed in 25 of the 394 patients who survived without amputation, and sequestration developed in 43. The tibia alone was broken in 87, and solid healing of these fractures required an average of 97 days, whereas, in the patients in whom both tibia and fibula were broken, solid union of the bones required an average

of 128 days. An average of 121 days was required for solid healing in the 45 torsion fractures, and 128 days in the flexion fractures. Healing depends not so much on the type of fracture as on the size and healing of the wound in the soft parts. It was found that, if lateral displacement of the fracture ends was more than one-fourth of the width of the shaft, not only was healing of the fracture retarded but pressure on the soft parts from the inside further retarded wound healing. Primary reduction is essential if the displacement reaches this degree.

Studies on the value of primary synthesis revealed that there was no difference in results from conservative treatment and from osteosynthesis. The number of pseudarthroses is much greater with osteosynthesis than with conservative treatment. Follow-up examinations were carried out 2 to 27 years after injury in 202 of the 456 patients with open fractures of the shafts of the leg bones. The gait was normal in 188 patients; a few required the use of a cane or orthopedic footwear. One hundred eighty had no complaints, and only 3 had serious complaints. Impaired functional capacity was reported more often in those with occupational injuries than in those with nonoccupational injuries. Most of those with occupational injuries received disability compensation, some temporarily and some permanently.

Results of Medullary Nailing of 65 Closed and 45 Open Fractures of the Leg Bones. W. Krösl. Monatsschr. Unfallh. (Supplement 54) pp. 181-206, 1957 (In German) [Berlin].

When Küntscher in 1940 advanced his idea of medullary nailing for fractures of the long bones, this method was tried at the Unfallkrankenhaus (accident hospital) in Vienna. From the end of 1941 to the beginning of 1944 this method was used in 110 fractures of the leg. These 110 cases accounted for 53% of all the leg fractures treated during that period. Since the results obtained did not come up to the expectations, the method was discontinued in the fractures of the long bones except in those of the femur. In closed or open fractures of the leg bones medullary nailing was abandoned, because the results obtained with it were inferior to those with the conservative method.

Critical Evaluation of Results of Treatment Between 1926 and 1950 at the Vienna Accident Hospital in 1,432 "Old" Closed and Open Fractures of the Shafts of the Leg Bones. H. Jahna and E. Scharizer. Monatsschr. Unfallh. (Supplement 54) pp. 207-227, 1957 (In German) [Berlin].

The authors speak of "old" fracture if the patient was admitted to the hospital more than 14 days after a closed and more than 24 hours after an open fracture. It was possible to compare the results of various forms of treatment in 480 of 863 patients with old closed and in 433 of 568 patients with old open fractures. The best results were obtained in the old closed fractures of the leg by primary traction with subsequent immobilization in plaster and in the old open fractures by primary traction and reduction with simultaneous immobilization in plaster. Primary surgical operations produced the poorest results in old fractures whether they were closed or open. The correct weight is of decisive importance during traction.

Diagnosis and Treatment of Acute Slip of the Femoral Epiphysis. E. Scharizer. Wien. med. Wchnschr. 107: 182-185 (March 2) 1957 (In German) [Vienna].

Epiphysiolysis of the head of the femur was treated in 30 patients ranging in age between 7 and 16 years. Twelve of these patients had acute femoral epiphysiolysis. Reduction or extension, of an insignificant slip was performed on 8 of the 12 patients under general anesthesia within the 1st week. Closed reduction with the application of a plaster spica was carried out in 4 patients, and 4 had nailing in situ with Kirschner's wire. Padded borders occurred in 2, and a temporarily increased calcification in the affected hip joint was observed in 1 patient. Follow-up examinations from 6 months to 16 years later showed that 3 of the 12 patients had marked necrosis of the head of the femur. Epiphyseal necrosis was produced in these patients by severe trauma, with primary injury of the vessels of the epiphyseal line and a marked primary slip, by additional injury of the epiphyseal line during forcible reduction under general anesthesia and by extensive injuries of the blood vessels of the epiphyseal line during treatment with the three-flanged nail. Nailing in situ after slow and gentle manipulation with traction appeared to be the treatment of choice in acute femoral epiphysiolysis, since it guarantees a good fixation and the children are not handicapped as by treatment with plaster spica. Nailing in situ did not damage the epiphyseal blood perfusion to produce necrosis. A normal anatomic condition after acute femoral epiphysiolysis could not be obtained.

The Gastroscopic Appearance of the Resected Stomach. L. Friedrich. Gastroenterologia 86:775-795 (No. 6) 1956 (In German) [Basel, Switzerland].

Of 5,000 gastroscopies performed because of postoperative complaints on 561 patients (452 men and 109 women) who underwent gastric resections, 2,042 were performed on 280 patients between 1937 and 1946 and 2,958 on 281 patients between 1946 and 1955. Of the 280 patients, 6 had Billroth 1 resections and 274 had Billroth 2 resections, and, of the 281 patients, 15 had Billroth 1 resections and 266 had Billroth 2 resections. Although the number of Billroth 1 resections increased in more recent years, this method is still used relatively rarely. A normal gastroscopic appearance was found in 5 (25%) of the 21 patients who had Billroth 1 resections and in 66 (12%) of the 540 who had Billroth 2 resections. Of the remaining 16 in the group of 21 patients, pseudo-polyps were found in 2, gastritis in 8, marginal ulcer in 1, formation of pockets in 2, isolated polyps in 1, adenofibroma at the stoma in 1, and a coarse pale mucosa in 1. Of the 474 patients who underwent Billroth 2 resections and in whom the gastroscopic appearance was abnormal, pseudo-polyps were found in 42.4%, inflammation of

the anastomosis in 8.7%, gastritis of the stump in 34%, jejunitis in 1%, ulcers in 7%, and formation of pockets in 7.1%. Unabsorbed suture material was found in 9.75% of the patients. In the roentgenogram, this finding will be an exceptional one. The suture material was observed at the anastomosis and also higher up. It might cause severe inflammation or abscess formation. Carcinoma of the stump was observed in only 2 patients. Other findings were isolated polyps in the central portion of the stomach and higher up, punctate hemorrhages, varices in the fundus, hyperemia, anemia, and grape-like polypoid structures that had resulted from suture. These changes are rarely if ever revealed by the roentgenogram. Gastroscopy should not, therefore, be a substitute for roentgenologic examination, but it should be used as an adjunct to it. With experience, the performance of gastroscopy of the remaining portion of the stomach after gastric resection is no more difficult than gastroscopy of the stomach before resection. Gastroscopy was performed with the aid of small amounts of tetracaine hydrochloride administered as a spray, without the development of undesirable side-effects.

Ileocystoplasty: Review of the Literature and Experimental Contribution. F. Siracusano and E. Manetti. Chir. ital. **8**:361-395 (No. 5-6) 1955-56 (In Italian) [Belluno, Italy].

Ileocystoplasty was performed on 9 large, female dogs, which were divided into 3 groups of 3 dogs each. All animals were put under closed-circuit general anesthesia after intravenous injection of barbiturates and endotracheal intubation. The intestinal mucosa was left in the dogs in the 1st group, and it was removed in the dogs in the 2nd group. The intestinal serosa was kept on the inside in the dogs in the 3rd group. All dogs except 1 that died of infection survived the operation and were killed 3 to 4 months later. The nitrogen, sodium, potassium, and chlorine levels in the urine changed markedly in the dogs in the 1st group. The urinary nitrogen level went up to 0.6 Gm. the 1st week after operation, the sodium content dropped slightly, and the potassium level increased moderately. Less marked variations were observed in the dogs in the second group; urinary nitrogen level was 0.52 Gm., potassium 5.1 mEq. per liter and sodium 137 mEq. per liter after the 1st week. Values returned to normal in both groups 4 weeks after operation. No variations in the electrolyte levels or in those of the urinary nitrogen were observed in the dogs in the 3rd group because of the absorption of the intestinal serosa. The histological examination showed that the muscularis mucosa was perfectly joined in all the animals. An initial neoformation of the vesical epithelium that lay on the serous stratum of the intestine was observed in the internal surface of the dogs in the 3rd group. Normal and metaplastic epithelium were observed in the dogs in the 2nd and 1st groups respectively. Cystographic examination showed that the capacity and distention of the new bladder were good. The authors believe that the best operation is one by which a part to be anastomosed to the trigonum vesicae is formed with a loop of the ileum opened and sutured on itself after the removal of the mucosa. The serosa can be either in the inside or in the outside, the latter is preferred when peritonization of the new bladder is not possible.

Traumatic Detachment of Epiphysis at Distal End of the Tibia and the Fibula. R. Bartl. Monatsschr. Unfallh. (Supplement 54) pp. 228-257, 1957 (In German) [Berlin].

A series of 232 patients with traumatic detachment of the epiphysis at the distal end of the tibia was observed at the Vienna hospital for accidental injuries between 1928 and 1953 inclusive. In 80% of the patients the detachment was due to indirect trauma. Detachment of the distal tibial epiphysis is relatively frequent, in that comparison of its incidence with that of leg fractures in patients under 18 years of age revealed a ratio of 1:4. Twenty-eight or 12% of the children with epiphysial detachments were under 10 years of age, 88 or 38% were between 10 and 14 years of age, and 116 or 50% were over 14 years of age. Although in the children under 10 the incidence was about the same in boys and girls, above that age the males greatly predominated. Of the total of 232 patients 180 were male and 52 were female.

Detachment of the epiphysis alone was the most frequent injury existing in 87 patients, and epiphysial detachment with fracture of the diaphysis existed in 83 of the patients. The male to female ratio in both of these groups was 4:1. Epiphysial detachment with fracture of the epiphysis occurred in 29 patients, with the same number in both sexes, but, of the 33 patients in whom the epiphysial detachment was combined with fractures of both epiphysis and diaphysis, male predominated over female patients in a ratio of 7:1. There were no children under 10 in the last 2 groups. Whenever there was displacement of the fragments, reduction was accomplished and controlled by roentography. Additional treatment consisted in the application of a walking plaster cast. Follow-up examination revealed shortening of the leg by 2 cm. in only 1 patient. Valgus or varus deformity was observed in 7 patients, but the angle was never greater than 10 degrees, the patients had no other complaints, and the deformity did not increase later. The relatively favorable results are ascribed to the careful reduction, and they also prove that the epiphysial line is not as sensitive to injury as is generally believed.

NEUROLOGY & PSYCHIATRY

Electrocardiographic Changes in Artificial Hibernation. A. Villamil, R. J. Franco, J. Clavijo and E. Martinez Zuviria. Am. Heart J. **53**:365-379 (March) 1957 [St. Louis].

Electrocardiograms were taken in 8 male and 2 female patients between the ages of 6 and 47 years who were subjected to artificial hibernation by the application of ice bags after administration of a "lytic cocktail" comprised of promethazine, diethylaminoethyl-thiodiphenylamine chloride (Diparcol), and chlorpromazine. Artificial hibernation was used prior

to a major operation in 5 patients, for the treatment of cranial trauma in 2 and for psychiatric disorders in 3. The patients were maintained in the state of artificial hibernation for from 2 to 6 days. Their temperatures were reduced to 30 C (86 F) or less. In 2 patients, axillary temperatures of 22 C (71.6 F) and 24 C (75.2 F), respectively, were obtained. Several electrocardiograms were taken in 8 patients at different temperatures varying from 38 C (100.4 F) to 24 C. The pulse rate increased during the induction period in all the patients and auricular fibrillation occurred in 1. Once hibernation was stabilized, the pulse rate decreased below the normal average and/or the one obtained in basal conditions. This decrease in the pulse rate was accompanied by a prolongation of the P-R interval and the QRS complex. The Q-T interval was prolonged in all the patients. This prolongation was closely related to the drop in the body temperature. Variable changes appeared in the S-T interval, slight elevation being the most common in marked hypothermia.

Contrary to the well-known risk of ventricular fibrillation associated with low body temperatures produced with different methods of hypothermia, the depression of the autonomic nervous system by the "lytic cocktail" combined with cold did not cause any severe arrhythmias. On the other hand, the sensitivity of the heart of the hibernated patient to a direct stimulus, such as the introduction of a catheter in its cavities, was not reduced since arrhythmias were produced by catheterization in these patients as in those not subjected to artificial hibernation. The electrocardiograms obtained in the patients subjected to artificial hiberation are considered characteristic, although they are similar in quality to those produced by quinidine and related drugs and to those obtained in patients with severe malutrition.

Brain Injury and Suicide: A Cerebropathological Problem. E. Sperling. Fortschr. Neurol., Psychiat. **25:** 179-194 (Feb.-March) 1957 (In German) [Stuttgart, Germany].

The author describes the cases of 7 men between the ages of 26 and 59 with brain injuries who committed suicide. Autopsy was performed in 6 of the 7 patients. Histories with data on the patient's psychic condition during life were available, and information was obtained from relatives, co-workers, and friends. The 1st patient, who had lost his father when he was a child and had to work when he was only 10 years old, committed suicide by hanging himself 10 years after he had sustained a grazing gunshot wound of the right side of the head in World War II. After the war he became a miner and was put in jail because of repeated robberies. A brain injury associated with predominantly psychomotor attacks and with an 80% reduction in the capacity for gainful employment was recognized on clinical evaluation. A personality change characterized by increased irritability, pronounced sexual impulses, and instability with regard to work became more and more notable. Suicide was committed without leaving a farewell note. Autopsy revealed an extensive defect of the white substance in the anterior portion of the right temporal lobe of the brain. Microscopic examination revealed rarefaction of the nerve cells of the cerebellum.

This case illustrates the 3 important factors that deserve attention concerning the relationship between brain injury and suicide, i. e., the personality of the patient before he has sustained the brain injury, the progression of mental changes from the psychopathological point of view, and the anatomy of the damaged tissues of the brain. The early death of the father suggested environmental impairment of the patient's development. Psychomotor attacks such as those observed in this patient may be associated with functional disturbances of circulation resulting in rarefaction of the cerebellar nerve cells, which are particularly sensitive to oxygen deficiency. The brain injury was to a large degree unilateral. The 2nd patient, whose right frontal lobe had been injured by a piece of a shell, was emotionally unstable before he sustained the injury, and the 3rd patient was an unstable psychopath before he sustained a gunshot injury of the head. The brain injuries of the other 4 patients also were injuries of the frontal and temporal lobes, which may be considered as a "functional unit."

The occurrence of the organic mental syndrome seems to depend not so much on the bilaterality of the inflicted damage as on the fact that it is sufficiently extensive. Psychopathologically, the higher mental functions showed "disintegration," with incoordination of the deeper personality structures becoming manifest. Emotional upset was caused by the most insignificant events in the emotionally unstable patients. It should be considered equivalent to an "impairment of the free will power." Besides that, the possibility of the occurrence of hallucinations must be considered in patients with injuries of the temporal lobes. The risk of suicide is great in personalities bordering on psychopathy. The suicide of persons with brain injuries like that of other persons should be considered as an emotive act that, however, always depends on a motive except in patients with productive semiconscious states. Microscopic examination of the brain is of great importance for the evaluation of the relationship between suicide and brain injury.

Mumps Meningoencephalitis: A Clinical Review of 119 Cases with One Death. H. B. Bruyn, H. M. Sexton and H. D. Brainerd. California Med. **86:**153-160 (March) 1957 [San Francisco].

The authors reviewed the records of 119 patients with mumps meningoencephalitis who were observed in the isolation ward of the San Francisco Hospital in the 12-year period, 1943-1955. Records in which the diagnoses at the time of discharge included mumps or infectious parotitis were studied, as well as those in which there was a diagnosis of encephalitis of unknown origin, or septic meningitis. The criteria for attributing central nervous system disease to mumps virus were: (1) parotitis or other salivary gland involvement typical of mumps or (2) a significant rise of either hemagglutination-inhibition antibody or complement-fixing antibody. Ninety of the 119 patients were under 20 years of age, and 65 of these 90 were

under 10. There were 84 males and 35 females. In 79 cases (66.4%) a diagnosis of mumps or of mumps encephalitis was made at the time the patient was admitted. It is emphasized, however, that, in the early years of the period covered by the present study, the possibility of central nervous system involvement in this disease was not often recognized and subtle symptoms were occasionally missed on admission examination. Correct diagnosis of "mumps encephalitis" on admission occurred predominantly in the last 6 years of the period. The diagnosis "possible poliomyelitis" was made on admission in 11 patients, in 2 of whom parotid involvement was present at the time the tentative diagnosis was made. The diagnosis of poliomyelitis in the face of parotid swelling dramatizes the all-too-common ignorance of the potentialities of the virus of mumps. In the differential diagnosis of the syndrome of "nonparalytic poliomyelitis," mumps should be considered as a prominent possibility even in a known poliomyelitis epidemic.

The 1st of the 4 case histories presented was that of a patient in whom salivary gland involvement appeared after the central nervous system symptoms. Two weeks before admission, a sibling had had mumps with bilateral parotid involvement. The 2nd case exemplifies mumps parotitis, without clinical evidence of central nervous system involvement and with cerebrospinal fluid changes consistent with mumps meningoencephalitis. The 3rd case is an example of pronounced meningeal involvement, without evidence of salivary gland infection, and the 4th was a fatal case of mumps meningoencephalitis. The authors emphasize that mumps is one of the most common viruses to affect the central nervous system and should be given primary consideration in the differential diagnosis of aseptic meningitis. Many cases of mumps infection do not involve the salivary glands. The course of mumps meningoencephalitis is usually benign, with fever and signs of meningeal irritation lasting less than 5 days. The findings in the cerebrospinal fluid are usually distinctive, with a leukocyte count of over 200 per cubic milliliter, of which 80% or more are lymphocytes. Sequelae, even of a minor nature, are rare, and death is extremely rare.

Electroconvulsive Therapy: A Controlled Study of Its Effects in Geriatric Patients. J. S. Hamlon and S. Atkinson. Geriatrics 11:543-548 (Dec.) 1956 [Minneapolis].

Indications for electroconvulsive therapy in emotional illnesses of the aged differ little, if at all, from those in younger age groups, but the selection of the responsive aged patient can be much more difficult, for his symptoms may represent a complex blend of organic, emotional, and attitudinal factors. A group of 36 patients, consisting of 18 men and 18 women past 65 years of age, were selected from new admissions to a mental hospital. The majority showed mental symptoms ascribed to processes of aging. They were given mental examinations, behavioral ratings, and clinical detemination of degree of arteriosclerosis. Twelve were given electroconvulsive therapy, 12 thiopental, and 12 sterile water intravenously. The treatment schedules were otherwise identical and lasted 3 weeks. One month after treatment, the examinations were repeated.

Electroconvulsive therapy did not significantly alter blood pressure level, it slightly improved memory-orientation faculties as measured by mental test scores, and it produced statistically significant deterioration in behavior. The deterioration was most noticeable as it affected dress, toilet, speech, and eating habits. The patients in the 2 control groups, on the other hand, showed some improvement in these respects. Women showed less deteriorating effects than men in most behavioral areas. The impairment ascribed to the therapy was more noticeable in the patients with the more severe degrees of arteriosclerosis. Although the deterioration was statistically significant, it was not such as to add to the practical difficulties of medical and nursing care. It, therefore, seemed inadvisable to withhold electroconvulsive therapy as a trial procedure, if the course is limited to 6 or fewer treatments given at the rate of 2 a week.

GYNECOLOGY & OBSTETRICS

Clinical Contribution to Problem of Hospital Infection and Bacterial Resistance to Antibiotics and Sulfonamide Compounds. T. Koller. Gynæcologia 143: 105-112 (Feb.) 1957 (In German) [Basel, Switzerland].

Today, the incidence of deaths caused by infection at the gynecologic clinic of the University of Basel, Switzerland, is only 0.06 per 1,000 among obstetric patients and 0.9 per 1,000 among gynecologic patients with preoperative and postoperative infections of the sex organs. The postoperative death rate due to pneumonia is 0.6 per 1,000. Between 1944 and 1948, the rate of healing by second intention of Pfannenstiel's incision after operation for myoma was 3.37% as compared to 1.49% between 1949 and 1953. The morbidity due to infection in the puerperium was likewise low; healing by second intention of perineal incision with secondary suture was observed in only 0.3% of all patients with episiotomies, and healing by second intention of Pfannenstiel's incision occurred in only 2.2% of the patients with cesarean section. In contrast to that, puerperal mastitis occurred in 2.3% of all the women in the puerperium, and an incision was required in 0.4%, including those patients who were readmitted for this incision after having been discharged. The incidence of mastitis in proportion to the other diseases of gynecologic and obstetric patients seems to be too high.

Infection in newborn infants represents a sensitive test for the present risk of exposure to the hospital environment. Of more than 15,000 infants who were delivered within the last few years, only 1 died of aspiration pneumonia, and the morbidity due to pneumonia was 1.9 per 1,000. Not a single death occurred among the new born infants with other infectious diseases, the total morbidity among whom was 6.1 per 1,000. It seems possible that even this morbidity could be reduced by still greater care with respect to asepsis and antisepsis. The incidence of inflammatory

diseases of sex organs has not increased in proportion to the total number of gynecologic patients in recent years, but there has been a definite increase in the total number of cases of mastitis, including cases of purely external origin, and there has also been an increase in the rate of incisions in women with mastitis associated with formation of an abscess. The amounts of antibiotics and sulfonamides used for prophylactic and therapeutic purposes at the gynecologic clinic in the last 6 years were, on the average, 1,000,000 units of penicillin, 0.25 Gm. of streptomycin, and 1.5 Gm. of sulfonamide per patient.

Perinatal Death from Fetal Exsanguination. A. B. P. Mitchell, G. S. Anderson and J. K. Russell. Brit. M. J. 1:611-614 (March 16) 1957 [London].

The risk to the infant's life incurred by damage to fetal blood vessels at cesarean section has been overcome, but the danger of fetal exsanguination from other causes still remains. The authors report on 9 cases of fetal blood loss associated with vaginal delivery. Small antepartum or intrapartum hemorrhage occurred in 8 mothers. The origin of blood loss was not appreciated until after delivery. Seven of the 9 babies died. In 3 blood was lost from ruptured vasa praevia. In 3 others the ruptured vessels lay at a distance from the cervical os and were associated with a velamentous insertion of the cord or a succenturiate lobe of the placenta. The mechanism of blood loss remained uncertain in 2 other infants, since placenta and cord appeared normal. A large fetal vessel in a normally situated placenta was damaged at the time of induction of labor with a Drew-Smythe catheter in another infant. Prompt blood transfusion saved the lives of 2 infants. The authors emphasize the need of a practicable, reliable, and rapid test to show if fetal blood is present in the vaginal loss, since reliance on clinical features does not give sufficient warning for prompt treatment to be undertaken. A rapid alkali-denaturation test is described. The routine use of such a test will enable the obstetrician to detect fetal blood loss earlier in cases of antepartum hemorrhage and lead to a higher rate of fetal survival.

PEDIATRICS

Results of Bacteriological Analysis of Human Milk and Its Consequences for Pediatric Practice. D. A. A. Mossel and H. A. Weijers. Maandschr. kindergeneesk. 25:37-50 (Feb.) 1957 (In Dutch) [Leyden, Netherlands].

The bacteriological analysis of 60 unselected samples of raw human milk obtained from healthy mothers revealed total bacteriological counts of up to 2.3×10^8 per milliliter and Escherichia coli counts of up to 0.6×10^8 per milliliter. Eighty specimens of human milk obtained from healthy mothers under aseptic precautions, immediately cooled to and stored at 5 C, and analyzed within 6 hours yielded total counts up to 1.9×10^6 per milliliter, E. coli counts of up to 0.5×10^3 per milliliter, Streptococcus fecalis counts of up to 0.6×10^4 per milliliter, and counts of Micrococcus (Staphylococcus) pyogenes var. aureus up to 0.2×10^6 per milliliter. These high bacterial counts seemed to originate from the microflora of the breast. Human milk with total bacteriological counts over 10^5 per milliliter should not be used for infant feeding, even after pasteurization, because large numbers of dead bacteria may exert a toxic or irritating effect on the alimentary tract of infants. Human milk with counts below 10^5 per milliliter should be pasteurized before use. High temperature and short-term pasteurization (30 seconds at 80 C) should be used for this purpose, in order to limit the inactivation of immune bodies, enzymes, and other factors in human milk that contribute to the alleged favorable effect of breast feeding.

Though the pediatrician may wish to feed raw human milk to infants, he should not do so—even when the milk is collected from healthy mothers by what appears to be a sanitary technique—unless a complete bacteriological analysis has shown that the milk is indeed wholesome. The bacteriological requirements for raw human milk are: (1) aerobic and anaerobic plate count below 10^4 per milliliter, (2) absence of coliform bacteria in 1 ml., and (3) absence of salmonella organisms in 100 ml. Lyophilized human milk tends to become rancid quickly and therefore, should be packed with special precautions.

Observations Made in the First Austrian Summer Camp for Diabetic Children: II. Report: The Course of Diabetes Mellitus During the Sojourn in the Summer Camp. W. Korp and E. Zweymüller. Wien. klin. Wchnschr. 69:112-118 (Feb. 15) 1957 (In German) [Vienna].

Forty children, 20 boys and 20 girls between the ages of 8 and 15 years, with diabetes mellitus spent a 4-week vacation in a summer camp on the outskirts of Vienna. The camp was organized according to recommendations for American camps of this type. The diet on which the children were placed contained from 1,800 to 2,500 calories; 40% of the calories were supplied by carbohydrates, 20% by proteins, and 40% by fats. Of the average daily amount (200 Gm.) of carbohydrates, which was divided in 5 or 6 portions, 25 Gm. was given in the form of fresh milk, fresh fruits, or simple desserts to make the diet more varied and more palatable. Extra amounts of protein and fat were given freely in consideration of the caloric requirements (increased physical activities), but none of the children were placed on the so-called free diet because of the difficulty of exact metabolic stabilization with this type of diet and because of its unfavorable late results.

At the beginning of the camp period the insulin injections were given by the physicians or by the nurses, but at the end of the camp period all the children but 1 had learned how to give themselves the injections. The daily dose of insulin varied from 12 to 84 units, with an average of 30.5 units for children with a shorter duration of the disease, and 45.3 units for those with a longer duration of the disease. Two daily injections of lente insulin or of a mixture of several long-acting insulin preparations proved highly satisfactory in children with a longer duration

of the disease, while optimal metabolic stabilization could be obtained with 1 daily injection of lente insulin in children with a shorter duration of their disease. Urinary sugar determinations were carried out 4 times daily, 3 times with the aid of polarimetry and 1 time with the clinitest.

The simplicity of these methods made it possible for the young patients to make these determinations themselves before the main meal and before retiring at night, thus warranting exact control of the diabetes. Metabolic stabilization remained unchanged in only 3 children during the entire camp period; slight changes in diet and insulin were required in 12 children; and radical changes with an increase in the insulin dose, change of insulin preparation, and reduced carbohydrate ration were required in 25. Physical exercise and exact metabolic control, however, made it possible to reduce the insulin dose and even to increase simultaneously the carbohydrate ration near the end of the camp period in a large number of children. The camp period also was helpful from the educational point of view in that it made possible a freer mental development of the children who learned to become adjusted to the requirements of their lives as diabetics without the exaggerated care they had received from their mothers.

Carditis in Early Childhood. I. Bor. Ann. pædiat. 187:399-424 (Nov.) 1956 (In German) [Basel, Switzerland].

Inflammatory diseases of the heart in infants are rare. Of 63 infants and children under 3 years of age who died at the pediatric clinic of Charles University in Prague and on whom autopsies were performed, myocarditis was found in 35, primary fibroelastosis in 14, secondary pericarditis in 8, and endocarditis in 6. Of the 35 children with myocarditis, clinical diagnosis of the disease was made in 7. Since most of the children were in a grave condition when admitted to hospital, this number is not small and shows that the clinical diagnosis of acute isolated myocarditis is possible. Dyspnea was the predominant symptom. Nine children had bronchitis. Most of the children were cyanotic. On admission, only 2 were unconscious, 10 were afebrile, and 34 had tachycardia. Roentgenograms revealed hypertrophy of the heart in 33 children. The increased size of the liver was an early symptom of cardiac failure. The sedimentation rate was normal. The electrocardiogram did not always show changes in the repolarization phase. Early diagnosis and admission to hospital are of utmost importance. Treatment was ineffective in the 35 moribound patients, but massive doses of strophantine (0.6 to 0.12 mg.) twice daily, and 0.06 to 0.02 mg. of digilanid per kilogram of body weight, given parenterally and according to the patient's age, were effective in others. The maintenance dose should be one-fifth of the initial dose. Corticotropin in doses of 3 mg. per kilogram of body weight may have a favorable effect on patients with interstitial myocarditis.

The clinical sign in the 14 children with primary fibroelastosis was the alternation of dyspnea with apparent repose. A systolic murmur was heard which made differential diagnosis from myocarditis possible, since such murmurs were not heard in patients with the latter disease. Treatment consisted of large doses of cardiotonics, oxygen, corticotropin, and antibiotics. Fibroelastosis is common in infancy. Secondary pericarditis was detected in 8 children. Symptoms always resulted from the primary condition, i.e., pleuropneumonia or general sepsis. The autopsy findings in the 6 infants with proved endocarditis varied widely. Two infants had verrucous endocarditis of the mitral valve. The presence of rheumatic carditis was confirmed by microscopic examination in 4. An increased sedimentation rate was an aid in differential diagnosis from acute myocarditis. The symptoms of rheumatic carditis in infants differ from those in patients in the older age groups.

Typhoid Fever in Children. J. K. Thanawalla. Indian J. Pediat. 23:421-424 (Dec.) 1956 (In English) [Calcutta].

One hundred eighty-nine children, 107 boys and 82 girls, with typhoid fever were treated at a hospital in Bombay in 1955. Of these, 52 were between 2 and 5 years of age, 126 between 6 and 10, and 11 between 11 and 12. Of 13 deaths (a case fatality rate of 6.9%), 4 occurred in children between 2 and 5 years of age, 8 in children between 6 and 10, and 1 in the age group from 11 to 12 years of age. Nine of the children who died were boys and 4 were girls, the case fatality rate being higher among boys. In Bombay, the incidence of typhoid fever is higher in the months of May and October. Relative bradycardia, observed in adults with this disease, was generally absent in the children. The typical "typhoid tongue" was observed only in patients with severely toxic reactions and in older children. The incidence of complications, such as toxemia, circulatory failure, rectal hemorrhage, meteorism, diarrhea, bronchopneumonia, and meningism, was higher in children than in adults. The case fatality rate, however, was lower in children than in adults, except for children with diarrhea and circulatory failure. Relapses occurred in 10 children (5.2%), none of whom died. Treatment consisted of the administration of chloramphenicol. Of the 189 patients, 147 with high temperatures or other complications were treated with this drug. Of the 147, 48 were given the drug in liquid form and 99 in tablets. When tablets were given, it took an average of 4.7 days for the temperature to return to normal, and, when liquid chloramphenicol was given, the temperature became normal within an average of 7.4 days.

DERMATOLOGY

The Behaviour of Radioactive Sulphur After Its External Application to the Skin. A. Scott. Brit. J. Dermat. 69:39-49 (Feb.) 1957 [London].

Sulfur is an effective agent in the treatment of various skin disorders. It appears to function as a keratolytic and as a stimulant, but the mechanism by which these actions are produced has not so far been explained. The author used the free elemental radio-

isotope of sulfur, S^{35}, (1) to demonstrate the absorption and localization of sulfur in the normal skin; (2) to observe any alteration in the behavior of the isotope in the presence of seborrheic dermatitis, acne vulgaris, and psoriasis; and (3) to demonstrate the effect of routine therapy of the lesions on the previously observed behavior of the sulfur. Tests were made on 70 persons: 12 of these served as normal controls, 18 had seborrheic dermatitis, 18 acne vulgaris, 8 psoriasis, and the remainder miscellaneous conditions, including eczema, lichenification, ultraviolet irradiation, and discoid lupus erythematosus. S^{35}, with its half-life of 88 days, was incorporated in a hydrous emulsifying ointment with 2% of stable sulfur. In the resultant preparation 100 mg. contained 5 μc of radioactivity. The ointment was applied with appropriate precautions to a 5 sq. cm. area of skin, and the skin was covered with a cellophane patch during the interval of contact. Geiger counting was used to obtain quantitative values and autoradiography to observe the localization of the material.

As shown by autoradiographic visualization, sulfur is able to penetrate readily through the normal epidermis. There appears to be no preferential site of absorption. S^{35} showed a difference in its behavior in the various dermatoses investigated. This alteration in site of localization and mode of distribution occurred in a predictable fashion for each type of disease and paralleled, in its return to normal, the clinical improvement in the lesion. On the basis of these tests there appears to be no abnormality, as far as the anatomic distribution of sulfur is concerned, in the uninvolved skin of the same patient or in the area of a previous lesion. Microscopic examination of the autoradiographs in these experiments demonstrated that in the normal skin and in the skin with lichenification, eczema, and discoid lupus erythematosus, the sulfur remained entirely extracellular, while, in patients with seborrheic dermatitis and psoriasis, it became intracellular. S^{35} has a striking tendency to concentrate immediately deep to the midepidermis. The location of the band thus formed is reminiscent of the so-called keratogenous zone of Giroud, which stains so densely for sulfhydryl groups. Whether this also suggests that sulfur is involved in an intracellular sulfhydryl-containing enzyme system and whether this is its mechanism of action in seborrheic dermatitis remain to be answered.

Observations on Steroid Therapy in Psoriasis. A. G. Fergusson and W. A. Dewar. Brit. J. Dermat. 69:57-60 (Feb.) 1957 [London].

The authors assessed the efficacy of steroid therapy in 14 patients with psoriasis, who were selected for this treatment because of the severity and the extent of the lesions. All except one of the patients were treated with intramuscular injections of corticotropin. Initial dosage varied from 100 mg. daily for 2½ days to 150 mg. daily for 28 days, and treatment was maintained with 20 mg. of the gel daily, except in the 1st patient in whom 20 mg. of the gel every 3rd day was adequate. Another patient received 60 mg. of prednisolone daily for 12 days and this was reduced to a maintenance dose of 20 mg. daily. In 3 patients treatment was discontinued because of complications. Agitated melancholia developed in 1 patient, but a psychiatrist did not consider this to be due to therapy. In another patient treatment was discontinued because of tiredness, weakness, and cyanosis, with a low serum potassium level due to lack of cooperation in taking potassium orally, but the patient made a good recovery from coronary thrombosis, and in 1 patient vertebral collapse developed.

Steroid therapy is by no means a completely satisfactory form of treatment for psoriasis. There may, however, be an initial response in chronic cases and in exfoliative states, arthritic symptoms may be greatly benefited and severe relapses are uncommon. Prolonged local treatment with its attendant discomforts is obviated, and a saving in clothing and bed-linen results. Conversely, the treatment is empirical and is apparently merely palliative in effect. Side-effects may be serious if prolonged use is necessary. It appears, therefore, that, although the present results are not entirely satisfactory, their importance lies in the demonstration that steroids exert a profound effect on inveterate cases of this disease. The authors believe that there is an indication for this form of treatment in such cases, especially when they are complicated by exfoliative changes and arthritis.

Dermatoses in Patients Receiving Chemotherapy for Systemic Tuberculosis. S. W. Becker and S. H. Mounce. A. M. A. Arch. Dermat. 75:333-344 (March) 1957 [Chicago].

Of 239 patients receiving streptomycin and/or isoniazid for the treatment of tuberculosis, 87 (37%) had eruptions characteristic of the neurodermatoses, including dry neurodermatitis, dyshidrosis, exudative neurodermatitis, urticaria, psoriasis, and pruritus. Reports collected from the literature revealed that both streptomycin and isoniazid are neurotoxic (or neuroallergenic). Association of the administration of such drugs with the appearance of eruptions thought to be of neurogenic origin strengthens the hypothesis that such eruptions arise by a nervous mechanism. This fact, while strengthening the concept of neurosomatic, as opposed to psychosomatic, disorders occurring in patients with overactive, oversensitive nervous systems, with insufficient sense of fatigue, seems to indicate that such eruptions can occur without psychic participation. A hyposensitizing course of injections of streptomycin failed in 1 patient. Similar reports by others suggest that an allergic mechanism of production of the eruptions could be hypothesized only by assuming that the nervous system is the shock organ. The exudative eruptions healed rapidly and those of the dry type healed slowly after cessation of treatment. Continued administration of the drugs, often necessary, introduced therapeutic resistance on the part of the eruption. Dermatoses produced by aminosalicylic acid (PAS) seem to be for the most part of an allergic nature. None of the neurodermatoses were seen to be caused by aminosalicylic acid.

UROLOGY

Conservative Management of Ureteral Calculi Without Use of Hazardous Instruments. E. Gartman. U. S. Armed Forces M. J. 8:313-320 (March) 1957 [Washington, D. C.].

Of 237 proved ureteral stones in 200 men and 18 women, 186 stones were passed spontaneously without accidents or complications, 38 were removed cystoscopically (33 on the first attempt and 5 on a second, or a later attempt), and 13 were removed by ureterolithotomy. Two of the 5 patients in whom two or more attempts were made to remove the stones cystoscopically had attacks of pyelonephritis after the unsuccessful efforts, but there were no accidents. A total of 15 attacks of pyelonephritis occurred among those patients in whom cystoscopic efforts to remove from the upper ureter, stones ranging from 0.6 to 1.3 cm. in diameter failed. A ureteral perforation almost occurred in 1 of these patients. One patient, a chronic stone former, died of renal insufficiency some months after the removal of a parathyroid adenoma. There were no other deaths. In handling stones endoscopically, cystoscopic foreign-body forceps were used or a meatotomy was performed with the aid of cystoscopic scissors, but no rigid or metallic instruments were used beyond visual range. For stones above the meatus variously sized catheters were used. The results obtained show that ureteral stones can be adequately and safely handled without the use of hazardous instruments.

Follow-Up Examinations After Prostatectomy. E. Weidner. München. med. Wchnschr. 99:252-254 (Feb. 22) 1957 (In German) [Munich, Germany].

Since 1949, the author performed prostatectomy in 88 patients, transvesical operations in 16, and Millin's retropubic procedure in 72. There were 4 postoperative deaths, 2 after each of the operations. Histological examination of the prostate revealed carcinoma in 4 of the patients, who were disregarded in the follow-up examinations carried out from 2 to 6 years after the prostatectomy. Seven of the patients had died, but only 4 of them of urologic diseases. Follow-up examination was possible in 55 patients. Because of the advanced age of many patients, it often proved difficult to obtain a survey over the entire period that had elapsed since the operation; many would only report on the last 2 weeks. It was found that 32 still had to urinate once or twice during the night, but many of these also received treatment for heart disease. Most of the patients reported that the urinary stream was of normal force. A mild burning pain was felt by many for several weeks after the operation, but only a few noted a slight turbidity of the urine. Rectal palpation often revealed dense capsular rests, strands, and scar tissue, but there was no relationship between these changes and micturition and urinary changes.

The decisive factor is the restoration of the excretory function of the bladder. Examination of the urinary sediment proved valuable. The 23 patients without sediment were also all free from symptoms. Even slight functional abnormalities, such as a weak urinary stream, were accompanied by the appearance of urinary sediment. The author believes that in the presence of sediment indicative of cystitis, cystoscopic examination is advisable. In this way vesical calculi were found in 1 patient 3 months after a prostatectomy. Examination of the sediment is a simple method enabling the practitioner to supervise a patient who has undergone prostatectomy. Some signs of urinary incontinence were present in 16 of the patients, some of whom stated that they had to "hurry" when the urge came to urinate. A sphincteral weakness persisted for several weeks after the operation in many patients. Two patients wore a urinal temporarily. Patients should be warned that during the first few days after the removal of the catheter, there may be an occasional involuntary loss of urine, particularly on arising in the morning. Treatment with a strychnine preparation is helpful in these patients. The author believes that, in view of the favorable results of prostatectomy disclosed by the follow-up studies, patients with enlargement of the prostate should be urged to submit to prostatectomy as the only reliable method of cure. Millin's retropubic approach is to be preferred to other methods of prostatectomy.

OTOLARYNGOLOGY

Our Experience with the Rosen Operation. C. Basterrechea Zubieta and R. Bertran Escanaverino. Rev. laryng. 78:23-30 (Jan.-Feb.) 1957 (In French) [Bordeaux, France].

The authors used the Rosen operation with certain modifications of their own to mobilize the stapes in 69 patients with otosclerosis. The tests used in selecting patients for this procedure should include audiometric tone tests, measurements of the bone-air gap, and the Rinne, Weber, Schwabach, and Gellé tests. The most important of these has proved to be the Rinne test with a 1,024-cps tuning fork. The results may be positive, negative, shortened, or equal. Any patient with otosclerosis in whom bone conduction is reduced by at least 45 decibels in one of the conversational frequencies (500, 1,000, and 2,000 cps) may be regarded as a candidate for the mobilization procedure, unless he presents special anatomic or pathological contraindications. The caliber and condition of the external auditory meatus should always be ascertained, because the operation should not be attempted, at least by the standard approach, when the meatus is very narrow. The incudostapedial articulation may be approached by 3 routes: transtympanic; transmeatal, with Lempert's incision, used by Rosen and co-workers; and the retromeatal, which is recommended when the external auditory meatus is narrowed and tortuous and when mobilization is to be performed conjointly with labyrinthine fenestration. Local anesthesia is preferable, because with it audiometric tests can be made during the operation and the patient himself can appreciate the improvement in his hearing. Various incisions have been tried, but, since their adoption of the omega incision de-

scribed by Goodhill, the authors have had no tears or perforations of the tympanum, which were fairly frequent before.

Mobilization of the stapes should be performed under strict visual control. The direct method, in particular, which may be tried if the indirect method fails, requires a perfect view of the stapedial footplate. The effectiveness of the mobilization is tested by whispering at various distances, reference being made to the preoperative tests; any blood that may have entered the eardrum is carefully aspirated; the tympanomeatal flap is replaced and fixed in position with a fibrin tampon; the meatus is packed with iodoform gauze; and dressings and bandages are applied.

The most serious complication is re-ankylosis, which usually occurs within 6 months, if at all, and which leads to a rapid and progressive loss of the auditory gain. Radiotherapy in anti-inflammatory doses and cortisone by mouth are now being used in an effort to prevent this complication. The results of the operation were considered good if the patient was conscious of the improvement in his hearing and if it represented a gain of at least 10 db. in the conversational frequencies as shown by the postoperative audiogram. Good results were obtained in 72% of 22 patients whose preoperative bone conduction levels were above 20 db. in the conversational frequencies, and in 25% of the 47 with preoperative bone conduction levels of less than 20 db.

INDUSTRIAL MEDICINE

Seal Finger or Speck Finger: A Clinical Condition Observed In Personnel Handling Hair Seals. J. M. Olds. Canad. M. A. J. **76**:455-457 (March 15) 1957 [Toronto].

Seal finger or speck finger (Scandinavian blubber-finger) is the idiomatic name for a severe type of finger infection found in seal hunters and workers in the seal fishery. Its etiology is unknown, but it is associated with the handling of adult hair seals. It manifests itself as a cellulitis that goes on to arthritis, with eventual joint dissolution and healing by ankylosis. The author was able to study this lesion in sealers in Newfoundland. He stresses that seal finger differs from the finger infections in fishermen and lobstermen. The 1st signs of seal finger are redness and swelling around 1 of the interphalangeal joints. The finger is very painful and throbs. As stiffness due to the soft tissue cellulitis increases, the skin becomes a shiny purplish red, tenderness is marked, and the finger is boggy to palpation. Frank pus is not present, and incision reveals only a serosanguineous discharge. The whole hand shows pitting edema but is not reddened. There may be a slight amount of lymphangitis and slight enlargement of the regional lymph nodes, but these do not suppurate. From the 1st week or so after onset, the pain and throbbing gradually decrease, but the finger does not improve; and usually between the 2nd and 3rd weeks after onset of symptoms, crepitation appears over the affected joint on passive motion. Radiographs taken at this time will show narrowing of the joint space and some degree of subluxation. Pain diminishes but swelling persists for months. In 4 to 6 months, the finger is usually healed, with complete ankylosis of the joint held in 30 to 40 degree flexion, and tends to remain a "cold" digit thereafter.

The author believes that seal finger is largely preventable by protection of the hands and care of any cuts and abrasions. Before the sulfonamide era, heat, splinting and amputation were the only procedures available. Sulfadiazine saved a few fingers. Later penicillin proved more effective and aureomycin still better. Sixteen to 18 doses of aureomycin (250 mg.) every 6 hours are usually sufficient. Amputation will be required in the future only if antibiotic treatment is not available early.

THERAPEUTICS

Acetophenetidin (Phenacetin) as Cause of Addiction and Disorders: Anemias with Heinz's Bodies and Interstitial Nephritis. S. Moeschlin. Schweiz. med. Wchnschr. **87**:123-128 (Feb. 9) 1957 (In German) [Basel, Switzerland].

Addiction to acetophenetidin (phenacetin) is one of the most frequent toxicomanias in Europe, being exceeded only by alcoholism and nicotinism. The author lists 30 proprietary preparations that contain acetophenetidin and suggests that the intensive advertising campaign for these preparations is one of the causes of their increased use. Other factors are the increase in neurosympathetic disturbances resulting from the rush and restlessness of present day living and the tension involved in piecework. Workers take tablets because they hope to increase their output. The tablets generally contain acetophenetidin in combination with caffeine and a sedative. The acetophenetidin counteracts feelings of aversion, headache, and indisposition, replacing them by a enuphoria; caffeine as a stimulant and analeptic compensates for fatigue; and nervous symptoms are reduced or eliminated by the sedative. Some persons actually do achieve an increase in ouput with the aid of these compounds, but this increase in productivity is soon replaced by the subsequent acetophenetidin "indisposition." The addict generally tries to counteract this by taking more tablets. From an initial daily dose of 3 or 4 tablets some go to 10 or even 30 tablets, that is, they take from 2.5 to 7.5 Gm. of acetophenetidin daily.

The abuse of acetophenetidin first causes persistent headaches, and, later, the large doses produce dizziness, stupor, and severe cyanosis. The example of coworkers and the fact that brands of acetophenetidin tablets are on sale not only in drug stores, chain stores, bakeries, and restaurants, but even in factory canteens are reasons why addiction is steadily increasing, particularly in the watch-making industry. It has been estimated that in some of the factories the consumption reaches from 5 to 15 tablets per day per worker. The early stages of addiction are usually characterized by a gray-blue cyanosis, with the signs of a toxic, hemolytic anemia, and the presence of Heinz bodies. The author is alarmed about the fact that interstitial nephritis is becoming more frequent in acetophenetidin addicts. Eight patients with severe uremia were

observed among 55 acetophenetidin addicts who were hospitalized in the course of 2 years. Four of these patients arrived at the clinic in the terminal stage of uremia and died, in another patient the uremia remained stationary, and the 3 remaining patients were improved. Complete withdrawal of the drug often reverses the nephritic process. The main findings in this form of nephritis are deficient concentration, with increase in urea and xanthoprotein, but only traces of or no proteinuria, combined with severe anemia. Pathological studies reveal chiefly tubular damage. The author recommends that acetophenetidin be obtainable only by prescription.

The Question of the Anabolic Effects of Isoniazid. G. Buchwald. Tuberkulosearzt. **11**:86-92 (Feb.) 1957 (In German) [Stuttgart, Germany].

An attempt was made to elucidate the alleged anabolic effects of isoniazid. The drug had no or insignificant influence on the blood sugar level. A slight decrease of the blood sugar level in the patients admitted to a sanatorium 3 months after isoniazid treatment was started had to be attributed to other factors. Patients with chronic tuberculosis had an increase in appetite and gained weight both under isoniazid therapy and under conservative treatment. Hyperorexia and, consequently, weight gain were observed in patients with acute exudative forms of tuberculosis, after treatment with isoniazid was started. These results suggest that the anabolic effects of the drug in patients with acute tuberculosis may be definitely considered as signs of recovery.

Continued Treatment for Chronic Myeloid Leukemia with Myleran (Sulfabutin). J. Beyreder and E. Herzog. München. med. Wchnschr. **99**:223-226 (Feb. 15) 1957 (In German) [Munich, Germany].

Sixty patients with chronic myeloid leukemia were treated with 1, 4-dimethylsulfonoxybutan (Busulfan [Myleran, Sulfobutin]). In 39 patients this drug was used exclusively; the remaining 21 had previously received radiotherapy. Average doses of 10 mg. daily were particularly effective when administered during the initial stage of the disease, but even patients who were resistant to radiotherapy responded well to the drug. It had no effect when given in the terminal myeloblastic stage of the disease. An attempt of continuous treatment was made with smaller doses, from 1 to 4 mg. daily or 2 mg. every 2 days, and several patients underwent this treatment for more than 22 months. Favorable blood pictures, regression of the splenomegaly, a good general condition, and a lasting capability for work were maintained. Long-lasting remissions for 3 years and more were the result of continuous treatment with the drug. An outpatient treatment was thus made possible. The hospitalization time was, therefore, reduced. Overdosage caused lesions of the bone marrow in 3 patients, but no significant untoward side-effects occurred in the other patients. The authors conclude that 1, 4-dimethylsulfonoxybutan is the drug of choice in the treatment of chronic myeloid leukemia.

Auricular Tachycardia with Auriculoventricular Block in Oleander Leaf Poisoning. Dao Chin and Ch'i Wei-Liang. Chinese M. J. **75**:75-77 (Jan.) 1957 (In English) [Peking, China].

The bark and leaves of the oleander contain active principles with a digitalis-like action. Its leaves have been used in China for the treatment of mental disorders, and several cases of oleander poisoning have been reported in recent years. This paper presents the history of a patient with oleander-leaf poisoning, who was found initially to have an electrocardiogram suggestive of auricular tachycardia with A-V block and later sinus rhythm with 2:1 A-V block. Oleander leaf poisoning closely resembles the effects of digitalis overdosage, but the rapid restoration of the marked electrocardiographic changes toward normal is quite different from that seen in digitalis poisoning and is probably due to the rapid clearance of the active principle of oleander leaves from the body.

PATHOLOGY

A Correlated Histochemical and Electron Microscopic Study of the Intranuclear Crystalline Aggregates of Adenovirus (RI-APC Virus) in HeLa Cells. D. P. Bloch, C. Morgan, G. C. Godman and others. J. Biophys. & Biochem. Cytol. **3**:1-7 (Jan. 25) 1957 [Baltimore].

HeLa cells in tissue cultures infected with types 3, 4, or 7 of adenovirus (RI-APC virus) were studied in order to correlate certain histochemical and electron microscopic findings. Adjacent thin (about 0.05 μ) and thick (2 to 4 μ) sections of osmium-fixed, methacrylate-embedded cells were cut. By mapping the sections the same cells could be identified with both the electron and the light microscope. Intranuclear crystalline aggregates, seen with the electron miscroscope to be composed of ordered arrays of viral particles, were found by means of the Feulgen reaction to contain desoxyribose nucleic acid (DNA). Desoxyribose nucleic acid is, therefore assumed to be a constituent of the viral particle. The virus appeared to develop from an osmiophilic Feulgen-negative matrix. Displacement of nuclear chromatin occurred during this process. A Feulgen-azure staining method was found to permit clear distinction between nuclear (host) chromatin (DNA) and the viral material in thick sections.

The Bacteriologic Status of the Pulp Chambers in Intact Teeth Found to be Nonvital Following Trauma. J. B. Macdonald, G. C. Hare and A. W. S. Wood. Oral Surg. **10**:318-322 (March) 1957 [St. Louis].

The contents of the pulp chambers of 46 teeth of children and young adults were examined bacteriologically after a blow sustained by these teeth. The teeth were not fractured but were traumatically devitalized as evidenced by discoloration or failure to respond to thermal stimulation, electrical pulp testing, or both. Aerobic and anaerobic cultures were made. Of the 46 teeth, 38 yielded bacterial growth. The number of bacterial strains recovered from an individual tooth varied from none to 6. A total of 71 strains were iso-

lated. The largest single group consisted of aerobic streptococci (20 strains). Next in order were micrococci (15 strains). Anaerobic cocci constituted the third largest group (12 strains). Twenty-three of the 71 strains were anaerobes. These findings show that bacteria can be recovered from the pulp chambers of most traumatically devitalized teeth even though there is no direct communication between the pulp and the oral cavity. It is postulated that most of these organisms reached the pulp from the gingival sulcus by way of the lymphatics and blood vessels of the periodontium.

RADIOLOGY

The Use of "Biligrafin" in Investigation of the Postcholecystectomy State: The Results in 224 Cholecystectomies at Saint Vincent's Hospital, Sydney. J. Fleming, R. J. Healey and J. H. Hood. M. J. Australia 1:197-200 (Feb. 16) 1957 [Sydney, Australia].

Iodipamide (biligrafin) was administered intravenously in the radiographic demonstration of the bile ducts and gallbladder. The authors describe the results in 224 cholecystectomies and report on the use of iodipamide in the investigation of the postcholecystectomy syndrome. Of 200 patients with severe pain before operation, 38 still complained of severe pain after operation. It was thought that a study of the biliary ducts in this group might throw some light on the residual symptoms, particularly when the findings were compared with those of a contratest group who were symptom free. At least 5 minutes is taken for the intravenous injection of 40 cc. of iodipamide. The following observations were made on the patients who were free from symptoms after operation: The bile ducts were dilated in the majority of these patients after cholecystectomy, the common duct averaging 1 cm. in diameter. In some patients the common duct was the same size as that seen in normal persons who have not undergone cholecystectomy. The medium appears in the duodenum in about 20 minutes. Pronounced tapering at the sphincter of Oddi in the dilated bile duct must not be taken as evidence of stricture. Cystic duct remnants were seen in 3 patients; and residual calculi were present in the common duct in 2 patients.

Studies with iodipamide were made in 30 of the patients with unsatisfactory results after cholecystectomy, and abnormalities were found in only 5 patients—cystic duct remnants were present in 2 patients, the bile duct was grossly dilated in 2 patients, stones were present in 1 patient, and delayed excretion of the medium to the intestine was seen in 2 patients. There seems to be no relationship between duct size and residual symptoms; large and small ducts appear with equal frequency in patients with and without the postcholecystectomy syndrome. It would be wise to search further for the cause of symptoms before exploring a duct on the evidence of dilatation during examination with iodipamide. Cystic-duct remnants likewise do not seem to cause symptoms. Although it was at first assumed that calculi would account for some of the residual symptoms, calculi were found in 2 patients who were free from symptoms and in only 1 patient with symptoms. This investigation did not support the contention that the most common cause of recurrent symptoms is a stone in the common duct. It is admitted, however, that failure to visualize a stone does not exclude its presence.

After describing the results of barium meal x-ray examination in the group of patients with symptoms, the authors comment on the exploration of the bile duct in the patients with jaundice. Only 18 of 57 patients with a preadmission history of jaundice had the duct explored, and a stone was found in 3. No stones were found in normal-sized ducts that were not palpable before the duct was opened. Of 19 patients who were jaundiced on their admission to hospital, 16 had the bile duct explored and stones were found in 8. Of the 3 whose ducts were not explored, a stone has been shown to be present in 1 since operation. Ducts were dilated and explored in 20 patients; in 10 of these a stone was found. Three of 36 patients whose ducts were explored died, and 2 of these deaths were probably due to the exploration, although no stones were present on exploration in these 2.

PUBLIC HEALTH

Prophylaxis for Ophthalmia Neonatorum: A Survey of Practices in Idaho. W. W. Benson, B. J. Foltz and F. O. Graeber. Sight-Saving Rev. 27:13-16 (No. 1) 1957 [New York].

In August, 1952, the Idaho Department of Public Health adopted a regulation that accepted a 1% solution of silver nitrate in wax ampules or penicillin ophthalmic ointment (100,000 units per gram) as the only germicides of proved efficiency in the prevention of ophthalmia neonatorum. A survey of the prophylactics used in Idaho in the period from 1950 to 1954 revealed that this regulation had little effect on the choice of agents used. Two years before its passage almost 20% of all newborn infants were already receiving penicillin as a prophylactic agent, in the year preceding its adoption almost 40% received penicillin prophylaxis, and in the year of adoption almost 72% received penicillin. In the year after the adoption of the regulation, the change in prophylactic agents used was negligible. In the 5-year period of study, the use of silver nitrate decreased from 11,072 in 15,666 births to 3,001 in 16,747 births—a drop from 70% to 18%. In the same period the use of penicillin increased from 18 to 72%. Physicians in Idaho do not agree as to the prophylactic agent of choice against ophthalmia neonatorum. The choice of an agent seems to be determined by the hospital staff rather than by the individual physician. During the study period 5 cases of ophthalmia neonatorum were reported to the state board of health. The disease is still occurring in Idaho, and the whole question of prophylaxis against ophthalmia neonatorum should be reevaluated.

BOOK REVIEWS

Clinical Electrocardiography: Interpretation on a Physiologic Basis. By Manuel Gardberg, M.D., Clinical Associate Professor of Medicine, Louisiana State University School of Medicine, New Orleans. With chapters by Richard Ashman, Ph.D., Irving L. Rosen, M.D., and Louis Levy II, M.D. Cloth. $12.75. Pp. 315, with 261 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1957.

This monograph represents the evolution of the theory of electrocardiography developed by Lewis and Wilson, as modified by Ashman and Bailey and interpreted by the author. It is a lucid presentation of one branch of the main stream of the evolution of thinking in electrocardiography. As such, it should be read by everyone professing to be a serious student of electrocardiography. Of necessity, the book is so complicated that the ordinary electrocardiographer and, particularly, the physician who uses electrocardiography for practical purposes without much concern about its theoretical background may find it difficult to follow. On several occasions the author presents assumptions, not yet fully established as part of his logical development of the subject, with the same degree of assurance as known facts. The ordinary reader may overlook this. There is great emphasis on the ventricular gradient, probably beyond its merit as a clinical tool. Nevertheless, the book is provoking, fascinating, and stimulating to anyone versed in the field. Some concepts presented by the author should be used more often by other electrocardiographers. Chapters 13, 14, and 15 seem to be afterthoughts and could have been omitted. It is hoped that in the second edition the author will change the objective (and name) of this book and aim it at the experienced theoretical electrocardiographer, for whom it is suited.

School Health and Health Education with Special Consideration of the Teacher's Part in the School Health Program. By C. E. Turner, A.M., Ed.M., D.Sc., Chief Advisor, International Union for Health Education of the Public, Arlington, Mass., C. Morley Sellery, A.B., M.D., Director of Health Education and Health Services, Los Angeles City Schools, Los Angeles, and Sara Louise Smith., M.A., Ed.D., Professor and Head, Health Education Departmnet, Florida State University, Tallahassee. Third edition. Cloth. $4. Pp. 466, wth 32 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1957.

In this third edition, two associate authors have joined the original author to form a writing team representative of medicine, public health, and health education. The volume has been revised, brought up to date, and personalized for the reader. The comprehensive text provides full and careful coverage of the various aspects of the school health program. After tracing the historical development of school health in this country, the functions and responsibilities of the "school health team" are outlined and the health aspects of school-community relations are discussed in detail. The rest of the volume is devoted to the particulars of arrangements for health services, provision of a safe and healthful environment, and development of an effective health teaching program.

The authors have included a vast amount of practical detail in this new edition. A more comprehensive use of illustrations than in the earlier editions helps in clarification and adds to the attractiveness of the volume. The book should prove helpful to school physicians and physicians serving on school health committees and to health and education department personnel.

The Principles and Art of Plastic Surgery. Volumes I and II. By Sir Harold Gillies, C.B.E., F.R.C.S., and D. Ralph Millard Jr., M.D., Assistant Clinical Professor, University of Miami School of Medicine, Coral Gables, Fla. Chapter on Anaesthesia by Ivan Magill, C.V.O., F.F.A.R.C.S. With foreword by Jerome Pierce Webster, M.D., Professor of Clinical Surgery, College of Physicians and Surgeons, Columbia University, New York. Cloth. $35. Pp. 317; 319-652, with 2472 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; 25 Hollinger Rd., Toronto 16, Canada; Butterworth & Co., Ltd., 88 Kingsway, London, W.C.2, England, 1957.

This new textbook is a dramatic departure from the routine academic type. It reads like a fairy tale. It is exciting to the point that one can hardly put it down. It is narrated by a man who had a liberal training in the use of the English language. He tells the exciting story of his pioneering in the field of plastic surgery. One's interest is captivated by tales of how he spent his leisure time. Although hundreds of illustrations are presented, the accompanying narration is always found on the same page as the picture being discussed.

The first chapter tells of Gillies' interest in and approach to the field of plastic surgery in World War I. With a few basic principles from which to start, by his personal ingenuity, he expanded the field to the point where many other reconstructive problems were solved. Very few of these 40-year-old contributions have been improved on today. Because of the need for a special type of anesthesia, Gillies worked out, with his personal anesthesiologist, I. W. Magill, what we now know as endotracheal anesthesia. Not only did Magill's contribution aid in the surgery of the face, but it subsequently made possible the present-day field of chest and heart surgery.

Numerous chapters cover the entire field of general plastic surgery. Many technical tips on the use of skin grafts and flaps and treatment for lymphedema; benign and malignant tumors of the skin; congenital deformities of the ears, nose, and hands; cleft lips and palates; and genital lesions are included. The section on the field of hand surgery is beautifully written. A chapter on legitimate cosmetic surgery is included, and the reconstructive surgery developed in two major wars is amply described. All through the text, the author gives credit to the many associates who have worked with him. This book is of great historical and practical interest. The senior author has had pleasure in his practice, and this in turn has been projected into his book. This textbook is a classic in English narration and should be of interest to everyone because of the enjoyable simple manner of scientific description.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUERIES AND MINOR NOTES

TREATMENT OF BARBITURATE POISONING

To the Editor:—*What is the best form of treatment for a patient, seen at home, who is comatose due to overdose of barbiturates? There is, of course, no oxygen available, but an airway and, in addition, ampuls of Benzedrine, caffeine sodium benzoate, epinephrine, Nalline, antibiotics, and Metrazol are carried by the physician. Should Nalline be used at all? What other drugs should be carried in the bag for these emergencies, especially if the patient (or his parents) refuses hospitalization? Is there a stomach pump available that would wash the stomach and draw up gastric contents? Is there an emetic that could be put in capsules of Tuinal, Seconal, or Nembutal that would produce no effect unless 3 grains (0.2 Gm.) of barbituate were taken?*

M.D., Wisconsin.

This inquiry has been referred to three consultants, whose respective replies follow.—Ed.

Answer.—The best treatment to be given in barbiturate poisoning as described for a patient first seen at home is as follows: Remove dentures (if present) and insert airway, with the patient kept on his side to maintain adequate air space. The intravenous administration of 0.6 Gm. of caffeine sodium benzoate is preferred and may be repeated at 30-to-60-minute intervals until the patient can be aroused. If this is not effective promptly and if the patient is in obvious need of oxygen, artificial respiration should be given. Caffeine is the most useful drug, since it is not a convulsant and is believed to make the respiratory center responsive to carbon dioxide. Nalline is not so useful in barbiturate poisoning as it is against morphine and its derivatives. If it is used, such large amounts are necessary that they in themselves may cause untoward effects.

In smaller communities, without hospitals, the nearest available source of oxygen should be known. Stomach pumps will clear the gastric cavity if the tube is of adequate (large) bore. Emetics, such as ipecac in 1-Gm. (15-grain) oral doses, have been recommended for combination with barbiturates, but, since individuals differ in response to hypnotics, there is no assurance that 3 grains may be the upper limit of safety.

Answer.—The treatment of barbiturate poisoning varies with the degree of intoxication. Mild barbiturate poisoning is characterized by impairment of mental ability and judgment, transient nystagmus on lateral gaze, absence of depression of the tendon corneal and gag reflexes, no significant depression of respiration and blood pressure, and, most important, easy arousability by mild stimulation. In such cases, gastric lavage should be performed if ingestion of barbiturates has been recent, with care being taken to prevent aspiration of gastric contents. There are probably no stomach pumps available that have any advantages over an ordinary stomach tube plus a large hypodermic syringe or rubber bulb with valves. The patient should be kept stimulated and should not be allowed to go to sleep until the effects of barbiturates have disappeared. Dextro amphetamine (Benzedrine) sulfate may be given if desired.

Moderate barbiturate poisoning is characterized by sleep or light coma from which the patient can be aroused by very vigorous manual stimulation, by cerebral electrostimulation, or by pentylenetetrazol (Metrazol). Signs include constant nystagmus, marked dysarthria, some depression of the tendon reflexes with intact corneal and gag reflexes, slow and shallow (but not periodic) respiration, and absence of shock. If possible, patients with this degree of intoxication should be treated in a hospital. Gastric lavage should be done if ingestion of the drug has been recent. Treatment consists of continued close observation, since patients may become worse and pass into the group with severe poisoning. As long as patients respond to vigorous manual stimulation or to electrostimulation, analeptics are not necessary. Of the analeptics, Metrazol is the most useful in this grade of poisoning. If the patient does not respond to manual stimulation or to electrostimulation, 5 cc. of a 10% solution of Metrazol should be injected intravenously at a slow rate. If the drug causes twitching and grimacing and if the corneal and deep tendon reflexes return, Metrazol is the analeptic of choice, and its administration should be repeated every 15 minutes until the patient responds to manual stimulation. Failure to respond to Metrazol classifies the patient as belonging to the group with severe poisoning.

Severe intoxication is characterized by coma from which the patient cannot be aroused by manual stimulation, electrostimulation, or Metrazol; marked depression or absence of tendon reflexes; absence of corneal and pharyngeal reflexes; markedly depressed and periodic respiration; and, possibly, shock. Severe barbiturate poisoning is a medical emergency and should always be treated in a hospital. Symptomatic treatment is far more important than analeptic therapy and should be handled as an anesthesiologic problem. The airway must be kept clear and respiration must be maintained manually with an automatic positive-pressure respirator or with an external (Drinker-type) respirator. Other measures include maintenance of

---

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

fluid intake, use of antibiotics, and prevention of damage to the skin over the bony eminences. For details, standard textbooks should be consulted.

The current trend is to avoid analeptic therapy, since Nilsson (*Acta med. scandinav.* [supp. 253] **139**:1, 1951) has shown that the use of analeptics increases mortality as compared with careful supportive and symptomatic therapy. If analeptic therapy is used, picrotoxin is the drug of choice in this grade of poisoning. The initial dose of picrotoxin should consist of 2 cc. of a solution containing 3 mg. per cubic centimeter. This should be injected intravenously at the rate of 1 cc. per minute. As the injection is being given, the patient should be carefully observed for muscular twitching and for the return of corneal reflexes. Injection should be stopped if either of these analeptic effects appears. If the initial dose of picrotoxin does not produce the desired effects, it should be followed in 15 minutes by a second dose of 3 cc. If the definite analeptic effect is not obtained with this amount, the dose should be increased in amounts of 1 cc. until 5 cc. (15 mg.) is being given every 15 minutes. If picrotoxin is used, one must have thiopental sodium (or some other injectable barbiturate) available, since convulsions, if they occur, must be controlled with barbiturates.

Metrazol would be the most useful of the analeptic drugs mentioned in the question. Nalorphine (Nalline) should be used only if it is suspected that the poisoning is due to opiates or to a mixture of opiates and barbiturates. Nalorphine is a respiratory depressant (unless respiration is already depressed by an opiate), and poisoning due to barbiturates alone would cause still further respiratory depression. If nalorphine is tried, the dose should not be more than 5 mg. given very slowly intravenously.

The only other drug that might be carried for use in barbiturate poisoning would be picrotoxin. As mentioned above, if picrotoxin is used, an injectable barbiturate must be available in case of an overdose.

Efforts have been made to develop combinations of barbiturates containing either ipecac or copper sulfate as emetics. None of these combinations has been proved safe or effective for the purpose intended.

ANSWER.—The proper place to treat a patient who is comatose due to barbiturate poisoning is in the hospital. Nevertheless, there are usually three problems involved in the management of these patients. The first problem is maintenance of the proper airway, the second is proper oxygenation, and the third is maintenance of the cardiovascular system. The maintenance of a proper airway involves several things. One of these, of course, is the prevention of obstruction of the airway, which frequently occurs in these patients due to the fact that they are areflexic and the tongue falls back on the pharynx, obstructing the airway. Another problem involved as far as the airway is concerned is the fact that these patients constantly give out secretions in the oropharyngeal area, since they are unable to swallow the secretions. Frequently these find their way into the tracheobronchial tree, giving rise to atelectasis, commonly termed hypostatic pneumonia. The second problem involved refers to the proper oxygenation of these patients. The fact that they are making an effort to breathe belies their ability to ventilate. The effort that these patients make to bring air into the tracheobronchial tree may give the person managing the case a false impression that the patient is ventilating properly. The fact remains, however, that the respiratory center of a patient in this condition is extremely depressed and the tremendous effort to breathe is due to utilization of his accessory muscles of respiration. In the majority of instances, after an airway has been established, an assistor may be needed to help ventilate the patient properly. The third problem, which is frequently neglected in these patients, is the maintenance of the cardiovascular system, which may deteriorate unless attended to. This deterioration is usually due to many factors—too many to be covered in this reply. The fact remains, however, that the vasomotor system and the heart will rapidly decline unless the proper treatment is instituted.

Several facts are obvious in the management of these cases. 1. There should be good, efficient nursing care, which may never be accomplished in a home. 2. Ventilation should be assisted whenever necessary and better oxygenation instituted. 3. The vasomotor system may have to be maintained with vasopressors in order to continue functioning efficiently. 4. Analeptics may have to be employed to help the recovery of the central nervous system, especially the respiratory centers, and probably the cardiovascular centers in the medulla. On the basis of these principles, an airway should be placed either orally or nasally and continuous suction of secretions maintained. The patient should be on his side, so that secretions will tend to gravitate toward the mouth instead of being aspirated into the tracheobronchial tree. A Levin tube should be passed to help empty the stomach contents. One hundred per cent oxygen should be given to the patient by nasal catheter or, if ventilation is deemed inadequate, by means of an intermittent-positive-pressure unit such as the Bennett, the Dotco, or the Emerson. These units will supply both 100% oxygen and humidity and will assist respiration. The Bennett unit, particularly, may be utilized as a respirator, should respiration cease.

Recently, some analeptics have been developed that are believed to be specific for the treatment of barbiturate poisoning. Examples are Daptazole and Megimide. Experience with the use of these drugs is rather limited and at present insufficient to draw any definite conclusions. Antibiotics should be given routinely to these patients. Should the patient not respond to this treatment after 48 hours and should the respiration remain inadequate, a tracheostomy may be necessary. The value of the drugs mentioned in the inquiry, such as Benzedrine, caffeine sodium benzoate, epinephrine, Nalline, and Metrazol, is questionable in this condition.

CANDIDA OVERGROWTH FOLLOWING ANTIBIOTIC THERAPY

To the Editor:—*What is the best method for treating labial, perineal, and perianal irritation, pruritus, and inflammation secondary to Candida (Monilia) overgrowth incident to Terramycin therapy? Previous therapy with hydrocortisone and later fludrocortisone with neomycin reduced the inflammation and stopped the pruritus but did not clear the basic cause. Nystatin (Mycostatin) has since been obtained, but in very small quantities. What is the most effective method of using this drug?*

Capt. Lawton V. Manderson, M.D.,
A. P. O. 9, San Francisco.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—Overgrowth of Candida in the mouth, vagina, and perianal region is very common following the use of broad-spectrum antibiotics. As a rule, this is not associated with any symptoms or objective changes, but occasionally the symptoms and signs mentioned by the writer may be marked and persistent. It is possibly an oversimplification to assume that moniliasis is the sole factor operative. Mycostatin is a very useful drug in such cases, although by no means always effective. It is important that irritant therapy, whether topically to the skin or in the form of douches, be avoided. It is obviously of importance to rule out any gynecologic condition that might contribute to the discharge. The judicious topical use of hydrocortisone or prednisone, along with a trial of Mycostatin, probably offers the best chance for cure. In occasional instances the severity and chronicity of the process may appear to justify a short course of systemic corticosteroid therapy. If the acute manifestations can be brought under control by this means, it may be possible to control the more chronic residual dermatitis. Vulvar and perianal itching are not infrequently perpetuated as a localized neurodermatitis after the original exciting factor has been removed. Under such circumstances, the trauma of scratching plus irritant or sensitizing materials, transferred to the area by the fingers, may produce a very chronic disease. There is no single method of management that is regularly helpful in all cases.

Answer.—In the experience of this consultant, use of the occlusive method of treatment on the hands, fingers, and upper and lower limbs considerably shortens the period of treatment, and this is the only method that will produce a cure in many protracted dermatoses. The advantages of the occlusive method are as follows. 1. Only a minimal amount of the product is needed. 2. Due to the steady contact, a quicker result should be obtained. 3. Less frequent dressings are necessary.

The affected areas should, if possible, be shaved or closely clipped for easier application of the salve and to prevent absorption by the hair. Mycostatin ointment is applied in a thin film and covered with Saran wrap or, if preferred, with cleansing tissue, which absorbs only a minimal amount of the salve. These coverings are fastened with cellophane tape and held in place by tight underwear or by a close-fitting cotton bandage or no. 5 Surgitube closed at the middle of the inferior border. This occlusive dressing may be changed daily or every two to three days. Mycostatin vaginal tablets or rectal suppositories may be used concomitantly. The suppositories may be prepared in the pharmacy from Mycostatin powder. The vial containing 2,400,000 units would provide 24 suppositories, each containing 100,000 units of mycostatin in a cocoa butter base, 30 grains (2 Gm.) each. If Mycostatin ointment is found undesirable because of its greasy plasticide base, the vial of the powder could be incorporated in Almay emulsion base or a similar nongreasy vehicle to make 24 Gm. of the salve. A much more rapid response may be obtained by adding 10 Gm. of prednisone (Meticorten) or a similar hydrocortisone-like product to yield 34 Gm. of salve. Oral administration of Mycostatin is not required unless there is a systemic involvement. Higdon (*A. M. A. Arch. Dermat.* 74:620-623 [Dec.] 1956) states that no improvement resulted in three patients with monilial intertrigo who took 3 tablets of Mycostatin, 500,000 units each, for five days.

THROMBOCYTOPENIA AND HEMORRHAGIC TENDENCIES

To the Editor:—*A 12-year-old girl developed a thrombocytopenic purpura about six months ago, with petechiae, gingival bleeding, epistaxis, and a platelet count eventually down to 30,000 per cubic millimeter. She did fairly well on vitamin K and vitamin C therapy, but three months ago started her first menstrual period and continued to bleed. Eventually a splenectomy was done. Her progress was satisfactory until another menstrual period started, which has persisted for about three weeks. She now has a platelet count of 30,000 per cubic millimeter and petechiae. How can this girl be kept from menstruating without sterilization?*

G. A. Hopkins, M.D., Fort Worth, Texas.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—It is evident from the data submitted that splenectomy was ineffective in correcting the thrombocytopenia and hemorrhagic phenomena. This raises considerable question as to whether the underlying disease was idiopathic thrombocytopenic purpura or whether the platelet deficiency was due to some other cause, such as undue exposure to a toxic chemical or drug, to infection, to some destructive process in the bone marrow, to abnormality in the spleen, or to some other idiosyncrasy. It is of the utmost importance to try to establish the underlying cause of the thrombocytopenia before undertaking steps to stop the menstrual cycle, since bleeding from other areas of the body will undoubtedly supervene at some future date unless the thrombocytopenia is corrected. In many instances a very careful and repeated meticulous history will frequently disclose the offending agent or cause. Interference with menstruation and sterilization, only as a last resort, should be considered, if undue bleeding from menstruation appears life-threatening.

ANSWER.—The failure of the platelets to increase and the return of the bleeding tendency after splenectomy may be encountered in about half of the individuals of this group. Some respond to corticotropin (ACTH)-cortisone type of drugs, but the result may not be obtained in all patients, especially after splenectomy. A careful reassessment of the bone marrow is warranted to note the condition and number of the megakaryocytes. If megakaryocyte material is present, it would be worth while trying preparations of vitamin E, 100 mg., four times a day. Since vitamin C had some effect, it may be well to try the effect of rutin, hesperidin, and similar substances, including moccasin snake venom (starting with high dilutions). It is assumed that no large accessory spleens were present. This may be checked by looking for Howell-Jolly bodies in the red blood cells. If they are present, one may assume that splenectomy was complete. Testosterone preparations may have some effect on the menstruation. Some patients improve with the use of pectin, 20 grains (1.2 Gm.) in capsules, before each meal and at bedtime. Calcium lactate, 1 Gm., three times a day, may have some effect on the fragility of the capillaries. Patients respond in different degrees to the same type of medication, and the prognosis is not always good.

BURNING SENSATION IN THE FEET WHEN STANDING

TO THE EDITOR:—*A 49-year-old woman has had burning sensations in the fore parts of her feet for several years, induced by walking a short distance or standing for 15 minutes. There are no disturbances of temperature or color of the feet, and the pulses are all readily palpable. It is noted that she manifests a tendency toward hammer toes affecting the four smaller toes of each foot. It seems that when she stands or walks the distal phalanges become strongly plantar-flexed, almost as though the tendons were becoming shorter as time goes on. When the foot is elevated, the toes can be stretched out normally and do not remain in the flexed position. The patient has a younger sister who gives evidence of Raynaud's disease. What might this condition be, and what might be done?*

Lewis I. Younger, M.D., Winona, Minn.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—The condition in the case described is both interesting and difficult to appraise. There seems to be no obvious solution to the problem. The symptoms that have been presented do not suggest occlusive arterial disease, and the fact that pulses could be palpated readily tends to confirm the impression that this woman's difficulty is not due to vascular disease. It is of utmost importance to conduct a very complete neurological investigation to rule out such conditions as syringomyelia, myelodysplasia, Friedreich's ataxia, and similar diseases of the spinal cord that can produce hammer toes. Definitive treatment will depend, of course, upon discovery of the cause of the condition.

ANSWER.—This problem is not circulatory. Pain in the feet or legs when the patient is standing is almost never the intermittent claudication characteristic of arterial deficiency, even though it also occurs when the patient is walking. Raynaud's disease is not familial. This sounds like a static foot problem. The patient probably has no metatarsal arch, and, when she is standing and walking, the toes go into extreme plantar flexion in an attempt to take weight off the metatarsal heads. The basic fault is weakness of intrinsic muscles of the feet that flex the metatarsal-phalangeal joints. Therefore, treatment would be use of a metatarsal bar or pad and active toe-grasping exercises.

MALARIA

TO THE EDITOR:—*Is the presence of malaria possible in a territory where no human being is present?*

M.D., Venezuela.

This inquiry has been referred to two consultants, whose respective replies follow.—ED.

ANSWER.—The species of the genus Plasmodium that can cause human malaria are P. vivax, P. malariae, P. falciparum, and P. ovale. Natural transmission occurs only through mosquitoes, which are the definitive hosts. The parasites of human malaria are remarkably species-specific with regard to the intermediate host. In the laboratory it is possible to transmit transient infections of human malaria to primates and vice versa by artificially high blood inoculations. The conditions for these experiments, however, are such as to eliminate the possibility of an animal reservoir for mosquito-borne infections of human malaria. Practically speaking, once human malaria has been completely eradicated from a given geographical area it will only reappear if reintroduced by an infected human. Malarial infections of other vertebrates (mammals, birds, and reptiles), however, may be present in such an area.

ANSWER.—It is assumed that the question refers to malaria in humans. The fact that malaria sometimes appears to have been acquired in regions apparently uninhabited by man has led to speculation that some of the lower animals may harbor the human species of malaria parasites and act as reservoirs of infection for man. However, the concensus today is that even monkeys probably do not play the role of reservoir hosts for human plasmodia. The human species of plasmodia may have evolved from species originally occurring in the lower animals, particularly from simian species. Some of the malaria parasites of monkeys bear a marked resemblance to the plasmodia of man, so much so that they appear identical. It is as yet uncertain how many of the described species of simian malaria are valid and also what, if any, is the relationship between species of plasmodia infective for man and those common to monkeys. The failure to produce convincing cross infection seems to indicate relatively stable physiological differences (species specificity), even though morphologic differences are within the range of strain variations.

All species of human plasmodia are transmitted by species of anopheline mosquitoes after a period of development in the tissues of the infected mosquitoes. Malaria infection in the mosquito is not congenital, but, once infected, a mosquito may remain infective for relatively long periods (90 days or more) under favorable microclimatic conditions. Under favorable conditions plasmodia may remain alive in the mosquito throughout the winter and complete their development in the insect in the spring.

Plasmodia of monkeys and bats are also transmitted by anopheline mosquitoes. Therefore, when anopheline surveys are conducted in forested regions where monkeys are found, it should be recognized that mosquitoes may be infected with species of plasmodia occurring in these animals rather than with those of man. It should also be recognized that unusually long latent periods may obscure the time and place of acquisition of infection.

PERSISTENT PAIN AFTER HERNIA REPAIR

To the Editor:—*Approximately six years ago a patient had repair of a left inguinal hernia. Postoperative pain in the repair area led to several more operations and, finally, to loss of the left testis. Local injections of procaine in the inguinal area ultimately led to a progressive subjective complaint of widespread body numbness. An infusion of 1% Pyribenzamine solution into the urinary bladder, because of impotence and bladder discomfort, further increased the numbness. Psychiatric evaluation supplemented by a Rorschach examination showed findings compatible with a somatization reaction. The possibility is being considered that the procaine or the Pyribenzamine could have caused a generalized end-organ reaction. Please provide information concerning this.*

Michael M. Gilbert, M.D., Miami, Fla.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—Neither procaine nor Pyribenzamine can "cause" a generalized end-organ reaction. The manipulations and suggestions on the part of the physicians may have established in the patient's mind the belief (which he was already entertaining) that something incurable had developed. It is in such cases as this that lobotomy is sometimes outstandingly successful. Drugs, electroshock treatment, and psychotherapy are unlikely to be of much avail. Should a paranoid attitude be manifested, this patient might become dangerous.

Answer.—The problem of persistent pain after inguinal hernia repair is a very real one. It usually seems to be due to the development of a neuroma on the ilioinguinal nerve. One of the tests in common use is that of procaine injection to corroborate the diagnosis of neuroma. The fact is well established that in patients sensitive to cocaine and its derivatives certain sensations develop in parts of the body distant from the site of injection, but no instance is known in which these sensations persisted. In other words, they were only of very short duration. It is seriously doubted that infusion of 1% Pyribenzamine solution into the urinary bladder played any part in augmentation of this patient's symptoms, and the patient's insistence is further evidence of the existence of a psychiatric factor.

On the basis of the information submitted, it would therefore appear that psychiatric therapy should be the treatment of choice if central nervous system involvement can be definitely ruled out. It is unlikely that it will be a simple matter to persuade this patient to accept this form of treatment since, in all probability, he will cling tenaciously to the idea that his troubles originated with the injection of the procaine and were augmented by the infusion of Pyribenzamine.

SCHOOL HEALTH EXAMINATIONS

To the Editor:—*In the routine school health appraisal of high school students, the examination should be appropriate for detection of those diseases likely to occur or be in their incipiency during the 12-to-18-years age period. Where can detailed information be obtained concerning either the expected health problems of this age group or the content of an appropriate screening examination for adolescents?*

Kenneth D. Rogers, M.D., Pittsburgh, Pa.

Answer.—The routine school health appraisal of high school students by the physician is not diagnostic in nature. It is a screening type of examination to single out those youths with conditions demanding further medical investigation. Much preliminary work should be done by the nurse and other school personnel. This consists, first, of taking of the health history, including information concerning teachers' and parents' observations and the student's health habits and immunization record. Second, it should include a record of height and weight and the results of screening tests of eyes and ears.

The physician checks and evaluates this information and interprets it for the nurse, pupil, or parent. He then proceeds to a routine medical examination to detect any signs or symptoms that may indicate abnormalities needing correction, advice, or further medical investigation. Such an examination includes a check on nutrition, skin, heart, pulse rate (resting and after exercise), lungs, posture, muscle tone, orthopedic defects, hernia, eyes and lids, ears, speech, teeth, gums, tonsils, nose, thyroid, lymph nodes, glands, abdomen, and nervous system. Depending on his findings during physical examination, the physician may wish to include certain laboratory tests, particularly urinalysis and routine blood tests. High school students should also have a tuberculin test, and reactors should have an x-ray of the chest.

Dr. L. M. Corliss of the Denver public schools reports that such an examination of 17,874 students revealed the following percentage of defects: poor health habits, 29%; heart murmur (functional), 16%; bad teeth, 15%; throat, 9%; skin, 9%; ears, 8%; nutrition, 7%; orthopedic, 6%; poor health conditions, 5%; cervical glands, 5%; eyes, 5%; genitourinary, 3%; nose, 3%; heart murmurs (organic), 2%; abdomen, 1%; and nervous system, 1%.

Among the suggested references are three pamphlets put out by the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association (Suggested School Health Policies, ed. 3, 1956; Health Appraisal of School Children, 1955; School Health Services, 1953). Several A. M. A. publications are also recommended: the reports of the Fourth and Fifth National Conferences on Physicians and Schools, put out by the Bureau of Health Education in 1953 and 1955, respectively, and "Periodic Health Examinations," 1947.

PROTEOLYTIC ENZYMES IN CHRONIC SUPPURATIVE OTITIS MEDIA

To the Editor:—*What is the present status of the use of proteolytic enzymes, such as Varidase, in the treatment of chronic suppurative otitis media with cholesteatoma? Can this material be used to aid in cleaning out the cellular debris and inspissated pus frequently seen in this condition?*

M.D., Oklahoma.

Answer.—Proteolytic enzymes, such as Varidase, are acceptable in the conservative treatment of chronic suppurative otitis media with cholesteatoma. It will be of help in cleaning out the cellular debris. Such conservative measures, however, are purely temporary, and surgical exteriorization is the final treatment of choice in most of these cases.

IMMUNOLOGY OF DISEASES RESEMBLING NONPARALYTIC POLIOMYELITIS

To the Editor:—*It is generally accepted that immunity against paralytic poliomyelitis may be acquired as a result of a mild attack of the disease and also that a number of other viruses cause diseases simulating nonparalytic poliomyelitis. Is it not conceivable that there may exist between some of the nonparalytic viruses and the paralytic poliomyelitis viruses a relationship similar to the one existing between vaccinia and smallpox viruses? If such a relationship were found to exist, might there not be a possibility of using such nonparalytic poliomyelitis viruses in the preparation of a live vaccine against poliomyelitis?*

M. Gruenbaum, M.D., New York.

Answer.—It is now recognized that a number of viruses, other than the three known immunological types of poliomyelitis virus, may produce infections which simulate nonparalytic poliomyelitis. For some years now there has been an increasing awareness that the mumps virus, for example, can produce meningoencephalitis and that primary infections of the central nervous system by this virus are not at all rare. Recently certain members of the Coxsackie virus group have been incriminated in the causation of aseptic meningitis, and even more recently, two members of the ECHO (enteric cytopathogenic human orphan) virus group, viz., types 4 and 6, have been associated with outbreaks of clinical illness resembling nonparalytic poliomyelitis. All the immunological evidence currently available, which is extensive, points to the absence of any antigenic relationship between the viruses mentioned and the poliomyelitis viruses. If an immunological relationship existed between these groups of viruses, inoculation with vaccines containing some members of these groups should, theoretically at least, serve to confer protection against all, or most, of the viruses within these groups. Despite the absence of an immunological relationship, it may prove desirable in the future to include some of the Coxsackie or ECHO viruses in poliomyelitis vaccines in attempts to reduce the morbidity of infections due to these viruses, assuming, of course, that overt Coxsackie and ECHO virus infections are sufficiently important numerically to warrant such steps.

ARSENIC IN ANIMAL FEED

To the Editor:—*Attention has been called to the fact that hogs, cattle, and other animals are frequently fed arsenic in their feed so as to stimulate the appetite. In addition, approximately 50% of all the hogs raised in the Midwest and large numbers of the cattle are said to be fed arsenic tablets by veterinarians, farmers, and other personnel for the treatment of "bloody scours," and this form of therapy continues in some cases for the lifetime of the animal. In view of the recent evidence incriminating small doses of arsenicals present in tobacco as being the cause of carcinoma of the lung in smokers, should not one be seriously concerned about the small doses of arsenic present in the meat eaten every day?*

R. R. Grayson, M.D., Perryville, Mo.

Answer.—Arsenic is a natural constituent of a number of foods. Studies have demonstrated that farm animals fed rations containing no added arsenic compounds accumulate a small amount of arsenic in the tissues. Before organic arsenic compounds were recognized as suitable growth promotants in the rations of poultry and swine, extensive studies demonstrated that there was no increase in arsenic residues in the edible portions of the treated animals, due to the added organic arsenic compounds, when the products are fed according to directions. These directions include instructions to discontinue feeding for a sufficient period prior to slaughter to permit tissue residue to drop into the normal range.

The following quotation is from a recent release of the National Academy of Sciences, entitled "Statement on What Is Known About Relationships Between Cancer and Food Additives."

> What is known concerning a definite relationship between ingestion of a substance and the subsequent development of cancer in man? Accidental repeated ingestion of "radium paint" or the use of so-called "radium water" has been followed by the development of cancer of the bone. The ingestion of certain aromatic amines, such as β-naphthylamine or 4-aminodiphenyl, through industrial exposure has been associated with the occurrence of cancer of the bladder. Epidemiologic evidence indicates that a prolonged intake of sufficient arsenic may result in development of cancer of the skin.

Do these materials occur in the food supply of the United States? Arsenic is the only one. It may occur in some foods in extremely small concentrations as a

pesticide residue and is normally present in certain foodstuffs which have received no pesticide treatment. Insofar as is known, there is no danger from the amount of arsenic likely to be consumed from these sources under ordinary conditions.

Organic arsenic compounds have also been demonstrated as being effective in the treatment of swine dysentery ("bloody scours"). The treatment, however, is given only over a short period of time (about one week), which does not result in any increased accumulation of arsenic in the edible tissues of the animals. There are no known reports that would suggest that the small amounts of arsenic which occur in various foods are associated with the development of cancer.

HEMOGLOBIN AND MENTAL RETARDATION

To the Editor:—*Please provide information regarding the level of hemoglobin, or other similar factors, which may influence the behavior of the mental retardate.*

Leopold A. Potkonski, M.D., Mont Alto, Pa.

Answer.—It is well known that abnormal hemoglobin compounds, such as methemoglobin and sulfhemoglobin, may be damaging to brain tissue through anoxia. In normal hemoglobins the only studies that this consultant is aware of have been in persons with Mongolism. Here the hemoglobin values are normal in the majority of instances, but a considerable number will be in the upper ranges—26% above average and 13% above normal. In athyroidism and hypothyroidism the hemoglobin values are low, usually between 60% and 80% of normal, but these are associated with erythrocyte counts of between 3 and 4 million, and anemia is a part of the disease. It might be assumed that a subnormal hemoglobin content of the blood, such as is found in anemias, would carry less oxygen to the brain of a mentally deficient individual. Actually the oxygen consumption of a normal adult brain is 7.43 vol. %. Himwich (*Arch. Neurol. & Psychiat.* **44**:1213, 1940) found the cerebral oxygen consumption in 14 children with Mongolism to be 4.76 vol. %; in 45 adults with Mongolism it was 5.62 vol. %, or a reduction of 24.4%. This would tend to show that the oxygen is used at a slower rate.

DYSPNEA AND HEART BLOCK

To the Editor:—*What would be the best treatment for a dissociation of the atrioventricular rhythm due to heart block in a 73-year-old man? His atrial rate is 75 per minute and his ventricular rate 43 per minute. The patient gets short of breath when he walks 10 steps. There is no cardiac decompensation while he is resting, but he has a moderate degree of emphysema and pulmonary fibrosis.*

Saul S. Trevino, M.D., San Antonio, Texas.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—The dyspnea on exertion may be due to the pulmonary emphysema and fibrosis, in which case therapy should be directed toward these conditions. There is no therapy that will reestablish a long-standing atrioventricular dissociation. Most people do not have symptoms with a ventricular rate of 43 per minute. However, it may be possible to relieve his symptoms by increasing the ventricular rate by using epinephrine in oil suspension, Isuprel, or Paredrine. In an occasional patient, large doses of thyroid will increase the ventricular rate.

Answer.—Shortness of breath on walking suggests that heart failure is present. This should be treated with digitalis and, if necessary, the other customary means, i. e., salt restriction and mercurial diuretics. In spite of the complete heart block, if there is heart failure the latter should be treated and there should be no hesitancy in prescribing digitalis. A ventricular rate of 43 beats per minute is not bad, and it would appear that, if the heart block has been chronic, no specific treatment for it is required. However, should the heart rate become slower or should symptoms of dizziness or syncope develope, then, of course, such drugs as Isuprel, epinephrine, or ephedrine should be utilized. The presence of emphysema or fibrosis is no contraindication for the foregoing therapy. Incidentally, it should be decided whether it is the lungs or heart causing the shortness of breath. If it is the former, heart failure may not be present.

ETHYLENE DISULFONATE

To the Editor:—*Please supply information concerning ethylene disulfonate.*

Sidney L. Cohen, M.D., Newark, N. J.

Answer.—Ethylene disulfonate has been the subject of considerable controversy. First, there is some doubt that a compound of the alleged structure of ethylene disulfonate exists. In view of the enormous dilution, 1 to 10^{-15} (one part in a million billion), it is impossible to analyze the commercial brand of ethylene disulfonate and find anything but water. Second, the theoretical bases which underlie the clinical utility of this compound are exceedingly doubtful. Third, the concomitant drug and dietary restrictions which are insisted on by the manufacturer seem totally irrational on the basis of present knowledge. But these points may be of practical importance, as they may explain some of the improvements that are occasionally seen after use of the article.

As far as its use in eczema in children is concerned, there have been favorable reports by Wasson (*Arch. Pediat.* **60**:511, 1943) and Bartlett (*Arch. Pediat.* **61**: 311, 1944). These reports are uncritical, and in neither were there adequate controls. Archibald (*Arch. Pediat.* **62**:219, 1945) came to the conclusion that any effect the product had was the same as that of distilled water. He pointed out that distilled water has been used in various conditions of allergy on a nonspecific basis with occasional good results, equal in percentage to those he obtained with ethylene disulfonate. In evaluating the result of treatment with this drug in eczemas or other allergic conditions, it should be recalled that the proponents do much more than merely administer the drug and also that a hypotonic solution injected intra-

muscularly will have certain nonspecific effects, which may occasionally yield a clinical result. Much of the pertinent literature is summarized in the report by the Council on Pharmacy and Chemistry in THE JOURNAL 131:1495-1499 [Aug. 31] 1946). During the past 10 years there has been no additional evidence to support the value of ethylene disulfonate from either the clinical or the theoretical point of view.

BURNING SENSATION IN THE FEET

TO THE EDITOR:—*Please describe treatment for burning feet so commonly complained of by older persons. Patients have not responded to vitamin B_{12}, Priscoline, or Nitrol Ointment.*

R. S. Srigley, M.D., Hollis, Okla.

ANSWER.—There is no satisfactory remedy for this condition. All physicians have to deal with it from time to time. Vitamins should be used if signs of neurological involvement are found. All sources of irritation of the skin of the feet should be avoided. Generous-sized shoes, nonirritant socks, and powder on skin and in shoes sometimes help.

ESOPHAGEAL DIVERTICULUM

TO THE EDITOR:—*A 70-year-old woman has a symptomless pecan-sized esophageal diverticulum. It was recently discovered at her annual check-up examination (because of a healed duodenal ulcer of 15 years' standing). There were also seen several very small diverticula in the lower intestine (barium meal). The esophageal diverticulum is opposite the aortic knob, with slight narrowing of the esophagus at the level and slightly below it over an area of 3 to 4 cm. The patient objects to biopsy via esophagoscopy. There are no other findings, and all previous x-rays show the esophagus to be regular in outline and position but slight calcification of the aortic knob. What, if anything, should be done in the absence of symptoms, and how much danger is there in waiting?* *M.D., Louisiana.*

This inquiry has been referred to two consultants, whose respective replies follow.—ED.

ANSWER.—An esophageal diverticulum is not a tumor and should not be subjected to biopsy. If there is a question of its being a diverticulum, the esophagoscopist should be able to decide whether biopsy would be indicated to diagnose malignancy. If it is a diverticulum, there is no need to do anything in the absence of symptoms, and there is no danger in waiting.

ANSWER.—A symptomless diverticulum in the thoracic esophagus merits no treatment. Slight narrowing of the esophagus opposite the aortic arch is normal. However, any suggestion of stricture formation in the esophagus of a patient in the eighth decade of life deserves attention; in such an evaluation fluoroscopic and radiologic studies could be very helpful in resolving whether the narrowing is merely anatomic. A rather common accompaniment of an esophageal diverticulum in this area is a calcified tubercular lymph node. In fact, traction occasioned by old inflammatory processes is believed to be a factor of importance in the genesis of such diverticula. The diverticula in the lower intestine presumably are in the colon and also are asymptomatic.

ANAPHYLACTIC RESPONSE TO STREPTOMYCIN

TO THE EDITOR:—*A 30-year-old man who has been treated with streptomycin intramuscularly for the last six months developed within two to three minutes of another injection severe pulmonary edema, cyanosis, shock, and near syncope. No previous idiosyncrasy or allergic reaction of any kind ever manifested itself before in this patient. Would this correctly be called an anaphylactic reaction? Only after the administration of epinephrine, aminophylline, and oxygen did this patient recover from his reaction. How often does this reaction occur, and what type of reaction is it if it is not anaphylaxis?* *M.D., Ohio.*

ANSWER.—The reaction which this patient developed is regarded as an immediate or anaphylactic type of response to streptomycin in an individual sensitized by previous injections. Such acute manifestations are not frequently seen in conjunction with streptomycin, where the delayed reactions are more common. There are no statistics available on the frequency of the immediate or anaphylactic type of response to streptomycin. However, a similar case in a nurse, who had been previously exposed to streptomycin in the course of her work, has been reported by Rosen (*J. A. M. A.* 137:1128 [July 24] 1948). This patient went into severe shock after an intracutaneous injection of 0.05 cc. of streptomycin (5,000 units), characterized by collapse, asthma, generalized itching, and rapid pulse.

POLYPLOIDY IN MAN

TO THE EDITOR:—*In the April 6, 1957, issue of* THE JOURNAL, *page 1310, appears a query as to whether colchicine, as given to patients with acute or chronic gout, may cause polyploidy, in this way detrimentally affecting the offspring of those who may be receiving this drug. The answers of the consultants were that there was no known induction of polyploidy in man after the administration of colchicine and that such a mutation was quite unlikely.*

A phase of this subject which was not considered was the possibility of inducing temporary sterility in males or female during the administration of colchicine for acute or chronic gout. The question is of increasing importance in view of the fact that daily prolonged administration of colchicine is now being recommended as a prophylactic measure against acute attacks of gout.

Since it is well known that colchicine inhibits mitosis, particularly of rapidly dividing cells, it is very possible on theoretical grounds that even the amount of colchicine given in the above situations may induce inhibition of spermatogenesis. Some experimental evidence is available to show that

there is an inhibition of spermatogenesis in animals during colchicine administration. There is no experimental work available, as far as is known, on the effect of colchicine on spermatogenesis in man. Such a research project is well overdue.

From clinical observation it is difficult to obtain satisfactory evidence. Most gout patients are in the middle and later decades of life, when procreation is less common. However, I cannot recall one case in which a patient taking prolonged colchicine therapy for prophylactic reasons induced pregnancy in his partner.

Edward F. Hartung, M.D.
580 Park Ave.
New York.

The above comment was referred to the consultants who answered the original query, and their replies follow.—ED.

TO THE EDITOR:—*Regarding the possibility of inducing polyploidy in man by the use of colchicine, the crux of the matter rests on the relatively small doses used therapeutically in man, as compared with the enormous doses which must be applied directly in plants or injected into animals to induce the changes which the correspondent fears. There is certainly no evidence that the therapeutic doses used in man have any effect on spermatogenesis.*

TO THE EDITOR:—*The theoretical possibility that small prophylactic doses of colchicine could inhibit spermatogenesis in man should be investigated. However, such a project would necessitate careful design to control and eliminate the many physiological, psychological, and nutritive factors involved. A direct measurement of the effect of colchicine upon spermatogenesis may then, in the properly controlled situation, yield useful information.*

TREATMENT OF PLAQUES IN EYELIDS

TO THE EDITOR:—*The query regarding treatment of plaques in eyelids in* THE JOURNAL, *April 27, 1957, page 1660, really refers to xanthelasma and not to "liver spots" as the answer assumes. These focal cholesterol deposits on the eyelids reflect an underlying error in lipid metabolism. Their proper treatment involves regulation of hypercholesteremia, if this is present, and a search for serious underlying diseases, such as atherosclerosis and xanthomatosis. Surgical removal has been attempted only later to find recurrence, presumably because the lipid metabolic error had not been attacked.*

William E. Connor, M.D.,
State University of Iowa,
Iowa City.

TO THE EDITOR:—*In* THE JOURNAL *of April 27, 1957, page 1660, is a query under the title, "Treatment of Plaques in Eyelids." The inquirer asks, "Is there any satisfactory treatment for the collection of cholesterol on the upper and lower eyelids?" He also adds, "The serum cholesterol level has not been determined, but there are no other signs or suggestions of hypercholesterolemia." Undoubtedly this physician is referring to xanthelasma, and, as nearly as we know, these lesions are not "liver spots," as mentioned by the person answering the query. Furthermore, the consultant suggests the removal of the plaques by burning with trichloroacetic acid. This is not a generally accepted method of treatment, particularly on the eyelids. While many physicians still use trichloroacetic acid as a destructive agent, they would be less apt to use it in this location.*

Xanthelasma has definitely been shown to be a familial problem and indicates a possible disturbance in cholesterol metabolism. As has been shown by many investigators, ordinary cholesterol determinations often do not indicate the disturbance that is present. This group of individuals are more prone to have, both in themselves and in their family history, not only atherosclerotic changes but also other disturbances of fat metabolism, including gallbladder disease and heart disease generally. Many of these lesions are effectively removed by plastic surgeons and still others by physicians using a fulguration spark or electric cutting current. Because the tissue is soft and redundant, the little scars are not very noticeable in this location. The plaques tend to recur and are definitely a reversible process. A low-calorie starvation diet will cause the lesions to recede, but, when the patient begins eating a balanced diet again, they usually recur. They are a most interesting and often neglected skin problem. The principal reason for their removal is a cosmetic one.

Roy L. Kile, M.D.,
Auburndale Doctors Building
Cincinnati 19.

CRANIAL INVOLVEMENT FOLLOWING NASAL INFECTION

TO THE EDITOR:—*The query regarding cranial involvement after nasal infection in* THE JOURNAL, *April 13, 1957, page 1415, is quite interesting. However, I would like to know why the second consultant believes that "several small transfusions should be given before operation." I find nothing in the query to indicate that the patient is anemic. Is this another example of transfusion for transfusion's sake?*

John H. Schaefer, M.D.,
525 S. Flower St.
Los Angeles 17.

The above comment was referred to the consultant who answered the original query, and his reply follows.—ED.

TO THE EDITOR:—*This is not a case of transfusion for transfusion's sake. The patient in the original query has been subjected to a great deal of traumatic surgery and severe infection over a long period of time. His physical economy and blood have been weakened by large doses of heparin and Dicumarol. In addition, further radical surgery upon his sinuses and periorbital tissues and possible incision of the dura mater and brain tissue were suggested. The loss of blood is bound to be considerable, and the best hematologists state that such a recommendation is a sound one.*